

RISKS AND IMPLICATIONS OF AIDS-HIV TESTING IN NONTRADITIONAL LABORATORIES AND IN THE HOME

HEARING BEFORE THE SUBCOMMITTEE ON REGULATION, BUSINESS OPPORTUNITIES, AND ENERGY OF THE COMMITTEE ON SMALL BUSINESS HOUSE OF REPRESENTATIVES ONE HUNDRED FIRST CONGRESS FIRST SESSION

WASHINGTON, DC, MARCH 23, 1989

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RISKS AND IMPLICATIONS OF AIDS-HIV TESTING IN NONTRADITIONAL LABORATORIES AND IN THE HOME

THURSDAY, MARCH 23, 1989

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON REGULATION, BUSINESS
OPPORTUNITIES, AND ENERGY,
COMMITTEE ON SMALL BUSINESS,
Washington, DC.

The subcommittee met, pursuant to notice, at 10 a.m., in room 2379, Rayburn House Office Building, Hon. Ron Wyden (chairman of the subcommittee) presiding.

Chairman WYDEN. The Subcommittee on Regulation will come to order.

Today, the subcommittee is convened to examine the potential and the risks of testing for the AIDS-HIV virus in nontraditional laboratory settings.

This is an issue of growing importance because of the increase in requests by manufacturers to market home test devices for use by those who wish to know whether they are carrying this deadly virus.

Last month, Dr. Frank Young, Commissioner of the U.S. Food & Drug Administration, announced that he would hold a hearing to examine his agency's policy with respect to the licensing of AIDS home tests.

AIDS threatens the lives of millions of Americans. Given this threat, it is the view of this Chair that the Federal Government has a moral obligation to assist medical science in bringing to bear all possible technological power against this dread disease. Any responsible initiative that holds promise in turning back the incidence of AIDS must be implemented by Government policy makers.

The Chair is convinced that in the hands of the untrained, the unscrupulous, and the insensitive, home AIDS testing can inflict considerable human damage.

In the hands of the untrained, there will be more inaccuracies in AIDS testing.

In the hands of the unscrupulous, these tests can be used to violate confidentiality and make a fast buck by exploiting the fears of our citizens.

In the hands of the insensitive, those tested may not receive good counseling, and the patients may quickly interpret results as a virtual death warrant.

Now, there is no question that evolving testing technology is driving both nontraditional laboratory and home test approaches in the diagnosing of AIDS.

A quick, relatively cheap screening test for AIDS, manufactured by Cambridge BioScience, already has been licensed by the FDA for clinical use. More quick test products are likely to follow.

Witnesses today will express concern that it may be difficult to keep this test out of the hands of unqualified persons. Some witnesses will say that has already happened.

We will learn today that the FDA already has told one Cambridge BioScience customer in Texas to abandon plans to use the screen in "improper" home testing. Another storefront laboratory customer faced action by the State of Florida for alleged violation of that State's AIDS testing laws.

These new diagnostic technologies are part of the drive behind entrepreneurial demands for home testing.

These kits already have a place in the health care industry today. They can be used by blood banks, by emergency medical technicians, and by physicians in their professional offices. However, Government and private industry must guard against their misuse by persons interested primarily in turning a quick profit.

The Chair would like to point out that the subcommittee staff has discussed these matters with Cambridge BioScience and their marketing arm, as well as with company representatives in Washington, DC. The firm and its associates have declined to testify at today's hearing, but the record should show that our report will be kept open for written statements which may be submitted at a later date.

This is the fourth in a series of hearings by this subcommittee on the quality of medical testing. In October 1987, this subcommittee revealed high rates of false positive and false negative results, particularly among low-risk groups. These came even under the best of HIV testing conditions at licensed, professional medical labs.

To quote a New York Times editorial citing this problem: "What should an enlightened society do about a health test that can do as much harm as good?"

The verdict is still out on the reliability of home AIDS testing. But the marketplace demand for a quick, anonymous answer to the AIDS question has not waited for a solution to the problem of inaccurate clinical laboratory results. The explosion in nontraditional testing activity has encompassed mobile labs, storefront diagnostic centers, and specimen-drawing facilities in health spas and massage parlors.

The American people have a right to expect that their Government will take responsible steps to make sure that testing in this critical health care field promotes good medicine and good science. This subcommittee intends to work closely with the Food and Drug Administration and with the private sector to assure that obligation is met.

[Mr. Wyden's opening statement may be found in the appendix.]

Chairman WYDEN. Our first panel today will consist of Dr. Frank E. Young, Commissioner, U.S. Food and Drug Administration.

Doctor, we thank you for your patience. Anybody who, from time to time, consults a newspaper or magazine knows that you have a

few things, noncontroversial matters, that you're dealing with, and we thank you.

Dr. Young, as you know, it is the practice of this subcommittee to swear all witnesses. Do you have any objection to being sworn today?

Dr. YOUNG. Absolutely not.

Chairman WYDEN. Please rise and raise your right hand.

[Witness sworn.]

Chairman WYDEN. If you would, please identify your colleagues, so when they speak, we will know a bit about their background.

TESTIMONY OF FRANK E. YOUNG, M.D., PH.D., COMMISSIONER, FOOD AND DRUG ADMINISTRATION, PUBLIC HEALTH SERVICE, DEPARTMENT OF HEALTH AND HUMAN SERVICES, ACCOMPANIED BY DR. PAUL PARKMAN AND DR. GERALD DONLIN

Dr. YOUNG. Thank you, Mr. Chairman. I am delighted to do so.

First, on my right is Dr. Paul Parkman. Dr. Parkman is an eminent virologist. In fact, he was one of the first individuals to develop the vaccine for measles that is now used throughout the Nation. He is a graduate of the Medical School at Upstate New York and is also Coordinator of our AIDS program at the Food and Drug Administration as well as the director of the Center for Biologics, Evaluation, and Research.

On my left is Dr. Gerald Donlin, from the University of Rochester, who is currently directing the Diagnostic Program for Diagnostic Devices in the Center for Devices and Radiological Health.

The two gentlemen have different responsibilities but both focus on diagnostic tests. It is Dr. Parkman's Center that deals with the tests that we are focusing on today, but many of the other tests that you have been concerned with in home testing are actually under the purview of Dr. Donlin.

So, I thought both would be appropriate to accompany me as resource individuals for you today.

I would like, sir, because I know your time is constrained, to introduce my testimony for the record, but to make a few points that I think might be helpful in looking at this.

As you on the subcommittee know, my field is the field of pathology and diagnostic medicine. So, I am no stranger to the concern of safe diagnostic tests.

I think these are the following issues that need to be addressed:

First, it is FDA's role to focus on the protection of the public and to ensure that safe and effective diagnostic tests are brought forward through our licensing or premarket approval processes.

As part of this process, as well, we do postmarketing surveillance for these tests, particularly on the tests in clinical laboratories in which reports come through the medical device reporting regulations and other mechanisms.

We also have good manufacturing practices that aid in assuring the safety of these tests. But really, nothing can substitute for well-qualified individuals using accurate, safe, and effective tests in diagnosis.

As a physician, I should point out that diagnostic testing is an adjunct to the total clinical impression that a physician gets. I

think we have gone, at some times, a bit far in thinking that a mere test can diagnose the condition.

It is the total appearance of the history, the physical examinations, coupled with diagnostic tests, that are meaningful.

If we look at the potpourri of diagnostic tests that exist, some exist for diagnosis, others for screening, and still others to monitor particular conditions.

In focusing on the safety and effectiveness of a test, I would like to call just one thing to your attention from my testimony, and that is that the performance of any diagnostic test is expressed by the sensitivity and the specificity of the test.

When a test is 100-percent sensitive, it will always give a positive result for those people who have the disease or the condition being checked.

When it is less than 100-percent sensitive, some people who have the disease will not test positive—these are the false negatives.

On the other hand, if a test is 100-percent specific, it will always give a negative test for those who do not have the diseases or the condition being checked.

When it is less than 100-percent specific, it will yield some non-specific results, and some people who do not have the disease will test positive.

Now, each of us doing diagnostic tests are vexed by this combination of specificity and sensitivity, and no test is 100 percent in this fashion.

The second point to emphasize is that the predictive values are influenced by the prevalence of the disease in the test population. The lower the number of truly infected people in a population, the higher number of false positive that will occur.

Therefore, in a screening test in a largely negative population, a number of false positive will occur, and thus, a confirmatory test is absolutely mandatory.

You made another statement, Mr. Chairman, in your opening remarks, which is very important, and that is that in this disease, unlike testing a person for high levels of cholesterol, there is a death sentence given with a positive test. Without the appropriate interpretation and counseling, the Food and Drug Administration is apprehensive that some individuals might not only have major psychological concerns but also might do themselves harm.

There is another part that is important and that is the sacredness of confidentiality.

We have, as you know, Mr. Chairman, had great concerns at FDA of our own records being made public. I do not know the security of some of the mail-in tests and how secure the results would be, or possibility of the misapplication of these simple tests to individuals at times of duress. These are very important issues that must be examined.

Accordingly, the Food and Drug Administration has taken a cautious approach here. We have felt that we could license and have licensed a number of tests to be done in hospital settings, to be done in doctors' offices, for professional use, and even in areas of field testing, where, with very careful evaluation, quick tests can be used. I look at these as particularly relevant in underdeveloped countries.

But in the case of home testing, we felt that we needed to do two things. The first is to hold a public hearing. Many of the questions that you asked are similar to our very own concerns. Therefore, on April 6 we will hold a hearing. We felt it would be prudent to analyze these concerns first and, after that, to address some of the issues as to how to evaluate these home test kits.

It is true that some have charged that this is folly or wrong on the part of the Government to hold up home test kits until we know how to evaluate them. But I would submit that caution at this time is prudent, that we do need to ensure that the right way to evaluate these tests is clearly understood.

I think the American people demand nothing less than a good test, an excellent test with high specificity and high sensitivity, and, if it is to move into the home market, then to move into the home market with all of the controls and all of the safety features that will guarantee the protection of the American people.

We need to do it expeditiously, we need to do it honestly and fairly, and that is the direction that the Food and Drug Administration is moving.

I would be delighted, Mr. Chairman, to answer any questions that you may have. I have not gone into detail on all aspects of my testimony, but I wanted to just hit the high points for your consideration.

Thank you.

[Dr. Young's statement, with attachments, may be found in the appendix.]

Chairman WYDEN. Doctor, thank you. Obviously you share many of the same concerns that I do with regard to this issue.

Dr. YOUNG. Absolutely.

Chairman WYDEN. Let me just ask a few questions.

You have noted, and I as well, that the FDA has taken a cautious approach with respect to licensing of the kits.

Is there, at this point in time, new evidence which would point to the fact that these kits are reliable?

Dr. YOUNG. I do not believe until the April 6 hearing that we will have gathered enough evidence to focus on that. It is clear in my mind that the kind of kit that Cambridge BioScience developed is a very fine kit. It is a kit that is a simple agglutination test, and there will be many tests like this in the future. But these tests require, in our opinion, a trained professional eye. These kits are not yet ready for the home market.

Now, it is possible also that there are ways in which one could collect specimens and then bring those forward and mail them into a laboratory. But there are some concerns here that we have. Can this sample be collected properly? Can it be identified properly? Will there be the appropriate confirmatory test and will the results be brought back in a sensitive fashion by an individual who can explain it?

I would say, Mr. Chairman, that there are very few tests in which you can substitute the professional judgment of the health professional looking at the entire picture with a mere test.

We do some of these in monitoring, and they are very effective—the glucose tolerance test, the urine strip test, that has been used to monitor glucose in the case of diabetes. But medicine is not to

the state yet where you stick your finger in a little tube with a stylet, get out some blood, put it into a test, and, automatically, like Star Wars or Mr. Kirk coming down with that fine doctor in the 25th Century, whatever his name is, and give an automatic diagnosis from a simple blood test. We are not there yet. We need the professional advice, and we need the hearing on the 6th to determine exactly what is going on.

Chairman WYDEN. But at this point in time, no concrete new evidence exists that would indicate that these tests are reliable. Is that correct?

Dr. YOUNG. Paul, would you like to comment on that? I do not think there is any new information since February—

Dr. PARKMAN. The Commissioner has said in his testimony, and I think it might be useful to clarify, that we are talking about two types of actions here. One is a real home test kit, a device that a person would use in the home and get an answer from, without anybody else being there. He would simply take a specimen and test it.

Chairman WYDEN. Known as the self-screen.

Dr. PARKMAN. Yes; somebody is doing a self-screen with some sort of device, and, at the moment, we have no evidence that such a thing has been developed, although we believe it is technically feasible to develop such a product.

Chairman WYDEN. So, we have then established on the first test, the self-screen, no new evidence exists at this point with respect to the reliability.

Dr. PARKMAN. For that particular kind of test.

Chairman WYDEN. With respect to the second test, if you could describe that, known, I gather, as blood collection.

Dr. PARKMAN. Yes.

Chairman WYDEN. Tell us what the status is of that with respect to new evidence.

Dr. PARKMAN. That test, which I think is clear to everyone, is done by obtaining a specimen and sending it off to a laboratory where it is to be tested. We specified there that it should be a licensed test.

We have not examined, since February 6, additional information.

Chairman WYDEN. In that context, people would be drawing their own blood, would they not?

Dr. PARKMAN. Yes; they would be getting their own specimen.

Chairman WYDEN. They would be getting their own specimen, and in that regard, at least at this point, no new evidence exists in that area either.

Dr. YOUNG. I hasten to add that since the February date we put the call out for the April 6 meeting.

Chairman WYDEN. Now, the FDA premarket approval process, of course, is a way for companies to air their concerns before the agency, is that not correct?

Dr. YOUNG. That is correct.

Chairman WYDEN. We are going to hear from one of our witnesses that the FDA refused to review the application—

Dr. YOUNG. That is correct.

Chairman WYDEN [continuing]. For a home testing kit. Is that because the agency had concerns about accuracy, confidentiality, counseling? Or what prompted the agency to take its position?

Dr. YOUNG. We were concerned with all of those. We felt that until we had a national forum so that we could discuss these issues and be sure that the test would be accurate, we would not know what needed to be done without putting a burden on the people, that should not be there.

I hasten to add that we are not robbing people of access to tests, because tests can be done in clinics under confidentiality, in a physician's office, and in a wide variety of ways. But it is with the home kit itself that we had some major concerns and felt that it demanded a broad analysis in public.

Chairman WYDEN. You mentioned one of the tests that was being used, I believe the Cambridge BioScience Fast AIDS Test.

Dr. YOUNG. Yes.

Chairman WYDEN. What is your evaluation of the accuracy rate of that home test? We have seen reports of various kinds of figures, but I would be interested in knowing the view of the agency with respect to the accuracy rate of that test.

Dr. YOUNG. Surely. I will make a general comment and ask Dr. Parkman if he could add further to that.

We feel that it is a very accurate test when done in the hands of a professional individual. The more inexperienced an individual is in seeing agglutination patterns and following it through, the more difficulty that will be, and the greater difficulties will be on the faintly positive where it is likely to overread these, and it would have to be picked up on the confirmatory test.

It should be viewed as a good, accurate, screening test. Paul, would you like to comment on a detailed figure?

Dr. PARKMAN. Yes; the sensitivity and specificity of the Cambridge agglutination test are both in excess of 99 percent, or 99.4 and 99.5 percent. The sensitivity is equivalent to licensed ELISA tests. The specificity is slightly less. I think it is 99.5 or so as compared with 99.7 for ELISA tests.

Chairman WYDEN. Well, I find that interesting. I have a story from the Wall Street Journal that indicates that the agency recommends that all positive results be double checked and that the concern was that it was not as reliable as the ELISA test. That was a piece in the Wall Street Journal, February 8, 1989.

Dr. PARKMAN. We require, and it is so recommended in the labeling for this product, that a confirmatory test be done. In fact, in blood banks where we regulate the test, we require an additional, more specific test such as the Western Blot to be done.

Dr. YOUNG. Mr. Chairman, I do think though that article did a disservice to the company and made it sound more inaccurate than the testing at FDA had, in fact, found it to be.

Chairman WYDEN. I wish to make no comment about the article or the company. I was interested in that quote from the agency and that is what concerned me, because it was the agency's comment saying that there were questions as to whether it was as reliable as the ELISA test. We appreciate hearing further views on this.

Dr. PARKMAN. Mr. Wyden, I think that one of the things that has been clear from the start on this type of test is that one needs to

evaluate the results very carefully. One needs some experience to evaluate the test properly. If you give this test to an inexperienced person to perform, the results you get will be less than optimal. In hands where people are experienced, it has a very high degree of sensitivity and specificity.

Chairman WYDEN. What is the agency doing to make sure it does not fall into unqualified hands? Because that, very frankly, is the Chair's concern. I think you were here for my opening statement, and the question is the untrained, the unscrupulous, and the insensitive. I mean, ideal conditions, physicians' offices, and the like, that is not what is being debated here. What is being debated is what is likely to take place in the reality of American homes.

What steps are being taken by the agency to ensure that these tests do not end up in unqualified hands, with people injured as a result.

Dr. YOUNG. First of all, in dealing with the unscrupulous, you and I both know that is something that is extraordinarily difficult to stamp out.

Health fraud is a business that is very alive and well. We do have a Health Fraud Branch within FDA, and we think that this is a significant activity, because there are \$10 to \$40 billion a year bilked from the American people by health fraud. That would be an area that we could look at here.

We also, when we have found problems, and I will submit some of these letters for the record, have taken action of a regulatory nature when some of these tests are used inappropriately.

We feel that the labeling must be followed. This test is very clearly labeled for professional use, and I will submit the labeling for the record.

[The letters and labeling material may be found in the appendix.]

Dr. YOUNG. Now, it is impossible to catch all of these individuals, so that the unscrupulous will, to some degree, get away.

The untrained is somewhat easier to deal with than the unscrupulous. There, there is proficiency testing. The test training actually is through a highly qualified laboratory director and supervisory technicians. At least that is my experience in the past.

So, that is, again, why we would like to keep it in the large laboratory and under a well-trained physician, as we move into this new area.

Chairman WYDEN. But at this point there are no controls over who actually buys and uses the tests, is that not correct?

Dr. YOUNG. We can take regulatory action if a test is being used in an extra-label use.

Chairman WYDEN. Only in that instance?

Dr. YOUNG. In that instance; yes. Paul, would you like to add to that?

Dr. PARKMAN. Yes; if I could speak to our understanding with the manufacturer of the test. The intention is to market it in the health care professional environment.

In addition to Dr. Young's comments, we do have the field part of FDA that deals in a number of regions with problems that crop up, and they have been advised to keep their eyes open and to investigate any circumstances where it would seem that the tests

might be offered for use in a circumstance which would be inappropriate.

Chairman WYDEN. Doctor, with respect to the issue of counseling, a number of people had said that telephone counseling, which is apparently the main route that would be used through these home test kits, is the same thing as suicide counseling, that someone is on the telephone and talking to someone to try to persuade them not to commit suicide.

It seems to me it is a completely different kind of matter, because suicide counseling, over the phone, is your only option. It is your only alternative, and that, in fact, you use it because there is nothing else.

It seems to me that it is not at all analogous to say that counseling with respect to a positive AIDS test is like suicide counseling because the fact is that there is an alternative, which is face-to-face counseling.

Do you generally share that view?

Dr. YOUNG. I generally share that view. I will be very interested to hear the comments on the 6th of April. But in my past experience serving as a medical school dean, I was very, very concerned with the way a message was delivered to a patient who was desperately ill.

If I were to tell you that you had cancer, and I had a medicine, by the time I said you have cancer, you would have stopped listening. If I did not have a chance to follow up and have some rapport with you, I would be very concerned about your being able to process and act on that information.

That is my professional opinion. I do want to hear from others on April 6 to be sure that I am not doing something that is unwise.

Chairman WYDEN. One other question if I might. There have been some companies, some manufacturers that I have found, frankly, very impressive in their proposals and their ideas. Some of them have been quite candid by way of saying that they think most of the people who have applied thus far have been relatively questionable, and if not irresponsible, pretty close.

Do you think that there have been a significant number of questionable applications and questionable proposals in this area?

Dr. YOUNG. Are you talking about home test kits?

Chairman WYDEN. Yes.

Dr. YOUNG. Or the diagnostics in general?

Chairman WYDEN. Home test kits.

Dr. YOUNG. I do not know whether I could answer that one without having the first-line experience. Let me ask Dr. Donlin, who has seen home test kits and devices very extensively and then Dr. Parkman who has seen them in AIDS. I have not reviewed the applications personally.

Dr. DONLIN. About 4 years ago, I guess when the concept first developed in entrepreneurs' minds, the questions were usually first addressed to my division, being the Division of Clinical Laboratory Devices. I must say I think those first proposals were poorly thought out, superficial, and really lacking in professional integrity.

However, I am sure that as the issues have been discussed professionally and among manufacturers, I think the—I have not seen

the submissions or the proposed submissions that have been before the biologics group, but I would hope that they have matured in their professional thinking.

Dr. YOUNG. Paul, can you comment on that from your biologics standpoint?

Dr. PARKMAN. Yes; I think that we have seen a whole range of proposals and ideas that have been tossed around from highly professional, large commercial companies down to smaller, entrepreneurial firms.

There is even a range of people who are interested on the small, entrepreneurial firms' side. So, we have a whole range.

I think when the issue first came up, there were certainly more entrepreneurs than there were old line, established firms.

Chairman WYDEN. Well, Dr. Donlin has said that initially your view was that a number of the proposals were poorly thought out, and lacked integrity.

I asked both of Dr. Young and of Dr. Parkman whether there was new evidence that would point to additional reliability, and they said that it was not available at this point.

So, would that not lead one to conclude that there really have been modest changes, if any, in the application?

Dr. YOUNG. Mr. Chairman, maybe I could help out on this by putting it into perspective.

I think initially when any particular laboratory test comes forward into a new market it would be predictable to be less sophisticated, and, until the market gets sophistication, the tests get refined, and then come forward. We have seen this repeatedly in a variety of tests.

The point that Dr. Parkman and I were trying to make is that, with regard to new information since February, the very reason for having the April 6 meeting is to get us up to state of the art. So, we really would not be able to make a complete statement to answer that in fairness to the sponsors, because we have not seen and really analyzed the data. We have been focusing on moving some of the other diagnostic tests forward, and we look at the April 6 meeting as a real chance to get on top of this again.

Chairman WYDEN. I am just anxious to see any evidence which would show significant reliability, because as I said, we are anxious to muster all technological power. But if Dr. Donlin tells me that the initial proposals, in his words, were poorly thought out and lacked integrity, and then we ask Dr. Young and Dr. Parkman about no new evidence, and until this forum I gather we will not have any new evidence. This leads me to believe that there still are concerns about poorly thought out proposals and the lack of integrity, and I will be anxious, both later today and working with you at the forum on the 6th, to see what new evidence, if any, there is. I think that is the fundamental question. As new evidence comes in, we have to take steps to act on it, and I am certainly interested in doing that.

Dr. DONLIN. Let me, if I may, put into perspective perhaps the timeframe that I am talking about as I alluded to in my answer.

It was about 4 years ago that these initial proposals were being discussed. These were even before submissions. These were basically telephone contacts from interested parties, and those were the

contexts in which I think there was superficial thinking and inadequate data presentation to document the reliability of these tests.

Certainly, at the time, perhaps 2 years ago when the regulatory responsibility was transferred to biologics, there may have developed some of the more sophisticated thinking in this regard. I would agree with Dr. Parkman and Dr. Young that as of February of this year, we do not know what the status of that is, and we are looking to the April 6 hearing to bring forward any evidence of reliability or documentation of that.

Chairman WYDEN. Dr. Young, one other question. What does the postmarket surveillance system do to monitor the safety and effectiveness of home test kits?

Dr. YOUNG. Home test kits are very poorly monitored during the postmarket surveillance. The type of things that we can see well would be things such as glucose monitors, and even there, there are difficulties. It is interesting to note that the glucose monitor problems are more in user capability than they are in the instruments themselves.

We have also had to debug or work with helping the manufacturers to debug some of the instruments.

Very rarely will a consumer report in a problem with a home diagnostic kit, particularly when they are only using it occasionally.

For example, in the pregnancy home diagnostic kits, we get very few reports on those, whereas a glucose monitor, which is used over and over again, we get adverse reports.

So, I would predict that when we approve any home test kit it is going to have to be done with two factors that we would rely on. The first would be the premarket evaluation, which is why we are being careful to look at the two types, the ones done by the consumer, him or herself, and the ones mailed in, and by good manufacturing practices where we can see that the kit is made according to the specification.

But I hasten to add that a poorly designed kit made according to good manufacturing conditions does not help much at all. So, we really need to look at the premarket approval. That is why we have put so much focus on determining how we should evaluate these by getting a national consensus.

I do believe that as time goes on there will be an improvement in these home diagnostic test kits. I do believe that it fills a unique need. But I also believe, as you said in your opening statement, that we have to be sure that when it is introduced it is reliable, that it is safe, and not misleading.

Chairman WYDEN. Doctor, you mentioned that health care fraud is regrettably alive and well. Is AIDS one of the leading areas now where fraud and questionable claims are being made?

Dr. YOUNG. Absolutely, yes; we have enlarged our entire focus here because, regrettably, when people are desperately ill, that is just the time that the charlatan can rise to prey upon the well-being or the poor health circumstance of desperately ill people. We have seen that with medicines. We have seen it with devices. One of the ones that was removed early was a home device that sold for \$400 that was to electrostatically shock out the virus particles from your living room so that you were not likely to be infected.

We have seen other pieces of cellophane or plastic sold to put over the mouth of a telephone receiver so that you would not get AIDS from that.

We have seen some medicines that have been less appropriate.

This is a field ripe for the plucking, regretfully. Our great concern is that people who are already desperately ill are not victimized.

On the other hand, our great concern, also, is that good medicines get out as rapidly as they can to the desperately ill, including AIDS. That is why under then Vice President Bush's initiative we have modified our regulations to get treatment IND's in and to expedite the process of bringing drugs to the desperately ill.

Chairman WYDEN. That really sums up my fears, frankly. I would only want to know, in addition, that given the concern about fraud and AIDS, would it not be fair to say that the prospect for fraud and exploitation is greater at home where there is less professional scrutiny than in a laboratory or other professional setting where there are licensed health professionals available?

Dr. YOUNG. It is hard really to answer that. Intuitively, one would think that direct sales to the consumer may well be within that area. But I would like to get more evidence on that.

Chairman WYDEN. I have considerable sympathy, and you and I have talked a lot about this on this resources question, for the agency. I think it would be helpful to know for the record how many people, given your tight budget, you have assigned to this health care fraud area, particularly as it relates to AIDS?

Dr. YOUNG. We have, and I will provide for the record, some information on that. But we have to, regretfully, move people around. Right now I have 15 percent of the entire field working on Chilean fruit, and I say this as a major problem. Because, as difficulties arise, we have to move people out. We have seen in the blood bank inspections alone, in Red Cross and other laboratories, we had to double that this year. That was very important because we found, for the first time, a license which we will revoke, as stated in my testimony, because, even under the best of conditions, in a diagnostic laboratory the work was not meeting standards. Therefore, when I have to divert resources to meet national emergencies and move as we are now from less inspecting of some of the blood banks even to meet emergencies, it is an indication, sir, that I have to work very carefully on the resources.

Now, on the health fraud, we are very interested in it, but I am afraid, given the choice as to whether to look at blood banks or emergencies of cyanide tainting of food, or health fraud, we would move the health fraud to the lowest category. I do not think it should be in that category, but it is a problem of, again, funding and the Congress deciding what should be done at FDA.

Chairman WYDEN. Is there anybody who works expressly now on these kinds of fraudulent—

Dr. YOUNG. Yes; there is a team that we have on this. I will provide the numbers and the deployment of these people, but, again, they are subject to being moved into any other spots because they are widely deployed in the field.

[The information may be found in the appendix.]

Chairman WYDEN. We have talked about this before, but I very much want to see more resources allocated for the agency. My own view is that is what the American people want. You can debate a lot of things about Government, but public health usually starts first.

I wish to assist you, and I think you will have a lot of bipartisan support on that.

Dr. YOUNG. Thank you, Mr. Chairman, for your support.

Chairman WYDEN. Before we let you depart, the Chair would be considerably interested in having a demonstration of that kit up there, and we need a good physician, and your name came to mind.

Would you be able to do that for the subcommittee?

Dr. YOUNG. I would be able to do that. I will use the positive and negative controls, and I will take my mike over so I can walk you through it while I am talking.

Chairman WYDEN. Good.

Dr. YOUNG. This is a test which is fundamentally an agglutination test. It can be performed in the laboratory quite readily. For those of us dealing with diagnostic medicine, one of the approaches that we like about an agglutination test is that it can be standardized to many of the types of tests that we are working with.

In this particular one, there is both a positive and negative control, and I will demonstrate using both of those.

It is a simple kit in that it has a capability of delivering, at the site which I am going to put this on, a standard amount using the dropper. So, you first add a known amount of the negative control which I am putting here and then a known amount of a positive control which I have there. In this process, one adds the latex beads. The positive and negative controls act as the way in which you would quality control the test itself.

It is imperative that any time that you do a diagnostic test that you are able to see the control itself. In this particular case, the advantage that one has is that the positive and negative control are on the same disc as the four tests that you are going to use.

I am adding now the latex agglutination material to this. Again, a squeeze is a measured amount that can be added here. There are two simple stirrers that are used here, and one mixes the material together.

Now, as I shake this for about 3 minutes, one should then be able to see the reaction taking place, and if this works in this environment as well as it did the time that I tested it yesterday, you should be able to see the agglutination pattern in about a 3-minute period of time.

One then essentially rocks this back and forth to allow it to agglutinate, and I will just do that and chat with you for this period while I shake.

One has fondly referred to this as the "shake and bake test."

Now, to just go a little bit further on laboratory tests, for quality control of any test when you run a series of diagnostic tests, you need a positive and negative control which this test provides, and you always run these type of controls when you are doing a test with a limited number of test specimens. In this particular card, there are four tests.

The advantage of agglutination tests is that, as you can see, this can be done without a complicated set of reagents and without a complicated set of equipment. I think this test was most appropriately used, not only in the blood banks here under good supervision, but it can be used in developing countries, because it has the potential of being used without an extensive amount of equipment, and I have been pleased to see that type of market develop.

It has also been tested inside here. But again you need to always have good and well-trained people to watch this.

As I said in my earlier testimony, where you are likely to have the biggest problem will be in the test on marginal positivity in which one could see some difficulties.

I would imagine I have now talked for about 3 minutes. With a little bit of luck, this should be ready.

[Pause.]

Dr. YOUNG. If you take a look through the magnifying portion of that, you will have to get quite close, and I am going to put it down. The difficulty is you do not have good lighting, so let me take this over here. It has to be in indirect lighting.

Now, leave it down and get indirect light against it. You have to go very close to it. Use this portion there. Can you see it? Can you see the clumping there? You can see that is homogeneous on that one there. OK? That is a positive and negative control. It does work quite nicely.

Chairman WYDEN. Dr. Young, let me just ask one other question with respect to this company that has been given the go-ahead.

A financial analyst said that there had been some difficulty reading the results, and that it was hard to make a determination of an AIDS positive or an AIDS negative, and that the company is working on a color-coded version so as to give different colors for different results.

Is the agency concerned about this analysis problem? Because this was something that was brought to our attention by some of the financial analysts following the company.

Dr. YOUNG. Let me make two remarks. First, I cannot speak to anything that is under development on penalty of going to jail, and I do not want to do that.

But second, let me make a remark in regard to financial analysts and the analysis of medicines and diagnostics.

I have been shocked and appalled by the speculation that moves up and down the stock of good companies. When we have a public meeting, where there used to be mostly scientists in the past, now it seems there are more financial analysts than there are scientists. They then run out to make a story of their interpretation of what FDA thinks.

I find the consistency of their thinking of what FDA thinks, and FDA's thoughts, to be marginal at best, scurrilous and irresponsible at worst.

I regret the type of speculation that I see, because not only does it do harm to the company, but I think it possibly defrauds the investors.

Just a short time ago, I do not remember the company, it was one that had a stock selling for less than \$1, moved up to \$16 to \$24, and then crashed down. There is a lot of manipulation, and I

do think that we have judged this test to be a good test. Dr. Parkman gave the sensitivity. Speculations, as you read in the Wall Street Journal, without a quote of an individual, should be looked at as not necessarily FDA policy.

It would be as if saying Congress says rather than a Congressman.

Chairman WYDEN. I think that is an important point, and simply, all we want to do is to get an assessment of what has been out in public.

Dr. Parkman mentioned a high rate of accuracy for that one test, and, in effect, there is one test that has met the threshold.

But it is my understanding that accuracy rates were considerably lower with less trained technicians, that there was evidence indicating that there was a 15-percent inaccuracy rate. Again, the concern would be that would be the more widely used sort of individual. That would be the person who would be most likely to use it. Is that correct?

Dr. PARKMAN. As I said before—and you are correct—the—

Chairman WYDEN. That is correct?

Dr. PARKMAN. No; let me finish what I was going to say, and that is you are correct that a person who is inadequately trained would be expected to get less satisfactory results with these tests. It is because of that the labeling for the test, which Dr. Young has said he is going to provide for the record, has a boxed warning. It says despite the fact the test appears simple, you need to know how to use it, or words to that effect.

It is because of that we advised the company, and they agreed, to provide a special version of the test that is a training kit with known positive and negative specimens in it for people to use in advance of their using the test for diagnosis.

Chairman WYDEN. Did you tell the company to do that after the lower accuracy rates came in?

Dr. YOUNG. No; well, we have told them that from the beginning. They knew that before they got licensed. Another thing about that, another point I would make about the accuracy business, is that there was a study done in Africa which raised this issue some months back. It was actually the test that was used there that was reported. They did not use the final test that was licensed, so there was some additional development that occurred between that time and the time the test was approved. There was a great deal of focus, obviously, now on recommending training for individuals and technicians who do the test in the medical environment.

Dr. PARKMAN. Mr. Chairman, if I could add, it is imperative in my experience in supervising laboratories for years that any test can be done poorly if the individual is not trained. That is why we had in-house training courses for our technicians. Our supervisory technicians went to do continuing education. No test is foolproof. You really need to have a well-trained person operating it. I would not want to distinguish this test separate from any others in that regard.

Chairman WYDEN. I think that my concern is that we do not know how trained and how expert these people are who are using the tests, and you agree with that.

Dr. YOUNG. Yes; in fact, one of the things that I have been concerned with, as you know, Mr. Chairman, is exactly how we do quality assurance in clinical laboratories in general.

Chairman WYDEN. That is the key. We do not know how trained and how expert they are, and yet, the figures that Dr. Parkman gave came from those who were very trained and very expert, and this subcommittee has been reading press reports of how much lower they are for people who are not trained and not expert. That is the Chair's concern. I think that is what this whole debate is all about: Seeing that these kits are in the hands of those who are trained and sensitive to patients' counseling needs.

Dr. YOUNG. It is in the blood banks where those concerns are so great and in the disease such as AIDS where the emotional burden of the actual diagnosis and the need to identify when a person wants an answer, a correct answer. Thus we must focus on it, and that is the reason for our hearing, and we are just as concerned as you are in trying to get the right answer. We do think it is manageable, and we pledge to do so.

Chairman WYDEN. I appreciate it, and I think the point that you made, Dr. Parkman, is one that I just wanted to have clarified for the record, because I know that the rates are high when people are highly qualified. We have established now that there is no way to assure that people are going to be highly qualified when they use them, and the figures indicate that the accuracy rates are not so high for people who are not highly qualified. I consider that an important point to set out for the record.

Dr. PARKMAN. Our responsibility, of course, has to do not only with products such as these, but the blood supply. I think, as Dr. Young made clear earlier, we are not primarily the agency that regulates clinical laboratories.

Chairman WYDEN. You all are absolutely right, and you have the pleasure of being with us today, and that is why these questions are being put to you.

I thank you, and I thank you for your concern. We will look forward to working with you closely in the days ahead.

Chairman WYDEN. Jean McGuire, executive director of the AIDS Action Council and chair of the National Organizations Responding to AIDS; Dr. Jose Szapocznik, professor of psychiatry, Center for the Biopsychosocial Study of AIDS, University of Miami, Miami, FL; and Dr. James Rundell, M.D., Department of Psychiatry, Uniformed Services University of the Health Services, United States Air Force; and Mr. Steve Smith, Human Rights Campaign Fund, Washington, DC.

We thank you all for your patience. Some of you have been before our subcommittee before. It is the practice of our subcommittee to swear all of the witnesses.

Do any of you have any objection to being sworn today.

Ms. MCGUIRE. No.

Dr. SZAPOCZNIK. No.

Dr. RUNDELL. No.

Chairman WYDEN. Please rise and raise your right hand.

[Witnesses sworn.]

Chairman WYDEN. We will make a copy of your prepared remarks a part of the record in their entirety. If you could summarize your views in 5 minutes, that would be very helpful.

Ms. McGuire, why do we not begin with you.

TESTIMONY OF JEAN McGUIRE, EXECUTIVE DIRECTOR OF AIDS ACTION COUNCIL AND CHAIR, NATIONAL ORGANIZATIONS RESPONDING TO AIDS [NORA], ON BEHALF OF GAIL HARRIS, PROJECT DIRECTOR, NATIONAL RESOURCE CENTER ON WOMEN AND AIDS, CENTER FOR WOMEN POLICY STUDIES

Ms. McGUIRE. Mr. Chairman, I am Jean McGuire, and I am the executive director of the AIDS Action Council and the chair of the National Organizations Responding to AIDS. I am here today in the stead of Gail Harris, who is the director of the National Resource Center on Women and AIDS. We are representing the interests of the National Organizations Responding to AIDS which is a coalition of over 120 groups who are working on developing the Federal response to the challenges of AIDS.

The NORA Prevention Task Force, which is known as the Coalition for AIDS Prevention and Education, welcomes this opportunity to comment on the issues relating to the licensing of home test kits for the AIDS antibody. NORA notes its serious reservations, and welcomes the fact that you have noted them likewise, about the licensing of a product which may have an adverse impact on the public health response to the epidemic, particularly in the areas of behavior change, mental health, and access to services.

We have attached for the record a statement that was developed in 1986 along with our statement today which was the first consensus statement on the appropriate use of the HIV antibody test and the inseparable need for quality counseling.

The statement argues that AIDS prevention requires behavioral change which can only be accomplished through education and counseling. Tools such as the HIV antibody test are an appropriate adjunct to a voluntary program of behavior change, but testing in and of itself is not a goal, never has been a goal, and should not be a goal. It is only as good as a prevention tool as is the education and counseling that accompanies the test.

Indeed, we have some data that in the absence of counseling, people who are tested continue to engage in high-risk activities. The marketing of a home test kit appears to reflect a completely contrary point of view which emphasizes testing possibly at the expense of counseling.

Our statement goes through to explore the different aspects of a good counseling and testing program that I welcome your staff to review at greater length.

In the context of counseling, informed consent is something that we consider absolutely crucial. It shows that the client has understood the negative social, legal, and psychological ramifications of the HIV test as well as its positive effects. There is no real procedure for informed consent in the context of an at home testing protocol.

Thus, many individuals who might be encouraged to test through provocative or enticing advertisements, and who may be affected

by some of the fraud that you referenced earlier, might only find out about the implications of the complex legal and social problems following the testing process.

One of the most critical issues around home tests is the ability of such a program to adequately meet the psychosocial needs of the tested individual. For some time now, we have been aware of the very serious psychological impact of finding your testing positive. Posttest counseling is designed to help address the adverse psychological reactions to a positive test.

Data has been accumulated over the last several years indicating that adverse social and psychological consequences are associated with knowledge of one's sero positive status and include severe depression, breakup of relationships, social isolation, and disabling levels of anxiety.

As most testing has been done throughout the country, however, the number of anecdotal reports of suicide have also increased, and as one of the other panelists will report, the incidence of suicide and suicide ideation in the HIV-infected population appears to be disturbingly high.

Given the psychological consequences, posttest counseling cannot realistically be achieved through anything less than in-person contact. We again appreciate the extent to which you have remarked on that issue so far. Whether the home test protocol can meet this pressing need remains unclear. Indeed, providers are even questioning the adequacy of the existing minimum standard of care which is a 1-hour posttest counseling session.

The manufacturers of home test kits have placed a great deal of emphasis on the value of the telephone counseling that they will provide to all test subjects. In a brief review of the literature that we have conducted, it appears that the data about the efficacy of the telephone counseling in general is spotty at best.

While numerous studies exist assessing non-HIV related telephone counseling programs through self-related support satisfaction scales, very few rigorous scientific studies involving the use of control groups or random assignment have been completed. This strongly argues that the efficacy of such programs remains in great question even outside of the concerns of HIV.

The linkage in the counseling process of the individual to primary health care support can be critical in terms of outcome for the individual. For many people at risk, the counseling session may represent one of the few or the only contact that they may have to channel them into meaningful health care options. This linkage has become increasingly important, as with the advent of AZT, we now know that it may be possible to use medical interventions to delay the possible progression of HIV symptoms.

Without the opportunity for interaction with the health care delivery system through the counseling process, there is no assurance that a patient with HIV infection would receive appropriate medical or psychological followup. With a home test kit, the patient or client may lose that opportunity for a well-structured linkage with the broader health care system. This problem may be particularly acute with the minority and poverty communities where the lack of access to preventive and maintenance health care services con-

tinues to be a major cause of greater rates of AIDS morbidity and mortality.

To a very large extent, there are several major fallacies behind the proposed promotion of the AIDS home test. The major problem is that in each of these cases, and you have noted this likewise, the argument, initially advanced, may on the service appear to address legitimate needs. But scratch the surface, and the problem is much more complex.

It is argued that the home test kits may protect the anonymity of persons who are too afraid to get a HIV test because of the stigma and discrimination related to AIDS. According to this line of reasoning, the home test kit may encourage persons, who otherwise might not test, to find out their status to go ahead and test in the home.

But the answer to this problem, however, should not be to encourage people to use a second-rate medical device. It really should be to ensure that HIV-infected individuals are not discriminated against or their confidentiality destroyed through the establishment of strong Federal policy.

This argument also presents problems from the health care perspective. If the infected individual is too afraid to interact with the health care system or to get tested, what is going to assure that same individual with a home test kit result will interact with the delivery system to protect their health and prevent further deterioration of their immune system?

Another argument advanced, advocates the lack of access to testing sites particularly to rural Americans. According to this argument, this situation demands greater access to tools such as the home test kits. Access is an issue, but the appropriate policy responses are to expand AIDS related services like anonymous testing which you have worked very hard on.

Finally, the proposition that somehow AIDS testing should be made easier is really quite dangerous. The AIDS antibody test is a very serious matter. It provides an indication about whether or not an individual is infected with the virus that can cause a deadly disease, that the person is probably infected for life, and that the person is contagious.

This kind of information is not to be treated lightly. An individual must have some kind of social support system to sustain such news. If no support system exists, then the health care personnel administering the test must provide some modicum of support through the counseling process. Otherwise, we are left with individuals learning virtually life and death news on the other end of a cold telephone line.

Thank you for the opportunity to testify. We look forward to working with you further on this issue.

[Ms. Harris' statement, presented by Ms. McGuire, may be found in the appendix.]

Chairman WYDEN. Ms. McGuire, thank you very much, and we appreciate your testimony.

Dr. Szapocznik.

**TESTIMONY OF JOSE SZAPOCZNIK, PH.D, DEPUTY DIRECTOR,
CENTER FOR THE BIOPSYCHOSOCIAL STUDY OF AIDS, DE-
PARTMENT OF PSYCHIATRY, UNIVERSITY OF MIAMI-SCHOOL
OF MEDICINE, ON BEHALF OF AMERICAN PSYCHOLOGICAL AS-
SOCIATION**

Dr. SZAPOCZNIK. Thank you. I am a professor of psychiatry, and I am the deputy director of the Center for the Biopsychosocial Study of AIDS at the University of Miami. I am also the director at the University of Miami of two other centers, the Spanish Family Guidance Center that works with the Hispanic community, and a Miami World Health Organization corroborating center in mental health and drug dependence that works with the World Health Organization.

I am a member of the congressionally mandated AIDS program advisory committee that advises the Secretary of Health as well as the Director of the National Institute of Health, and I am a member of the AIDS policy subcommittee for the National Advisory Council of Mental Health which is part of the National Institute of Mental Health.

I am testifying today on behalf of the American Psychological Association and its 90,000 members which are involved in all aspects of HIV and AIDS work. As a behavioral scientist, my objective today is to summarize and to interpret the available evidence that might be relevant to the use of the home AIDS test kit for the promotion of changes in unsafe behavior which is one of the claims that have been made.

The primary purpose of my testimony is to address the safety and the efficacy of the AIDS home test kit as an instrument for changing unsafe behaviors that place individuals at risk of contracting the AIDS virus.

With regard to efficacy, I think that it is very simple. I am not aware of any studies investigating the efficacy of the AIDS home test kits in bringing about a change in unsafe risky behaviors. In general, the value of testing alone has been found to be very questionable.

In fact, there are data that have been obtained from individuals who were screened out of the enlistment of military services because of their HIV status. These individuals were not given any kind of counseling. They were just told that they were HIV positive, and thus they could not be enlisted into the service. A follow-up survey with the individuals who were sero positive showed that they continued to engage in high-risk behaviors. Thus, testing alone did not result in safer behaviors.

I think that we are on very strong grounds to state categorically that the efficacy of the procedure under discussion has not been established, certainly in terms of its use for changing risky behavior.

Then not having established that there is efficacy in the procedure, our primary concern was then turned to safety. In this regard, we have a number of studies that while not conclusive would suggest that the AIDS home test kit without counseling may be detrimental in several respects.

There are two different ways in which the AIDS home test kits could be detrimental. One, which perhaps may be a little surpris-

ing, is that it may actually encourage rather than discourage unsafe and risky behavior, and I would like to talk a little bit about this in a minute.

Chairman WYDEN. Doctor, let me just ask that because we have Dr. Rundell and other witnesses, if I can keep you to 5 minutes. That will be important. We will make a copy of your prepared remarks a part of the record in their entirety.

Dr. SZAPOCZNIK. All right. There are two different ways in which the test may be detrimental. One is that it may actually encourage rather than discourage risky behavior, and two, as it has been mentioned, it may have deleterious psychological and biological effects.

With regard to the first aspect that it may actually encourage risky behavior, social psychologists know that individuals have a great capacity to perceive themselves as uniquely invulnerable to negative consequences of external events. This is particularly the case with individuals tending to engage in high-risk behaviors such as adolescents and drug abusers.

We are also very aware of the power of selective attention. Individuals who perceive themselves as invulnerable are likely to extract from a situation the evidence that supports their belief that they are invulnerable.

Imagine then an adolescent who has recently engaged in unsafe behavior or an intravenous drug user who has recently engaged in unsafe needle sharing. Without adequate guidance and counseling, these individuals use a home test kit, they test themselves and find themselves to be negative, and they may interpret this as meaning that they are invulnerable, which is part of their belief system.

The fact is that they have been lucky in their game of Russian roulette, and I think that it is very crucial that without adequate counseling and guidance that these individuals are likely to attend very selectively to that notion that supports the belief of invulnerability. Without counseling, we cannot challenge that erroneous belief.

The second concern about the safety of the home test kit is that without counseling there are both psychological and biological detrimental effects. There is a very interesting and very carefully and well designed study by Professors Fletcher and Schneiderman at our university in which they randomly assigned individuals who did not know if they were positive or negative to a psychosocial stress reduction intervention or to a control condition where they only got the usual kind of HIV antibody counseling.

What happened was that the individuals who turned out to be positive responded very, very differently if they had been in the stress reduction intervention, or they had just received the usual kind of HIV antibody counseling. In particular, the individuals who did not receive much more than the usual counseling showed very high levels of distress, of anxiety, of depression, but they also showed immunological impairment as compared to individuals who got counseling and stress reduction. Those individuals not only have much lower levels of distress but immunologically they were doing much better.

So, this brings us a new field that is of great interest in psychology today, the field of psychoimmunology which says that the

impact of stress on individuals who are immune, well, all individuals and particularly individuals who are immune impaired, is very important to what their eventual health outcome might be.

So, very quickly to summarize, we are saying that there is a lack of available information on the efficacy; that there is a concern about what will happen without counseling, because we actually may be achieving the opposite of what we want; that we will be reinforcing erroneous beliefs; and also that we think that the minimum kind of counseling that is done today may not be sufficient.

I would like very quickly to talk a little about what we do know about counseling. There are a number of strategies that have been found to be effective. Researchers at the University of California have found very, very effective educational and prevention strategies. In fact, some of the strongest effects ever found in major community health interventions have been found with the community education programs in San Francisco.

There are individuals who do not respond to these kind of broad community education programs, and there is further research that has shown that skills training is particularly helpful in getting people to change their risky behavior. This may be particularly important for women who may require in addition to the usual information because they have to prevail on their partners in order to be able to engage in safe sex.

Finally, I would like to make a comment about intravenous drug use, because this is also an area of great concern to us. The individuals who have been working in this area such as Dr. Schuster who is the director of the National Center on Drug Abuse, and Dr. Delargie who is probably the best recognized authority in the world in this area, both have concluded in review of studies with intravenous drug users that there are effective strategies for changing intravenous drug users, particularly where alternatives are available.

So, in conclusion, I think that what we would like to say is that when there are efficacious alternatives for changing risky behavior, it would perhaps be unwise of us and maybe even irresponsible to approve something such as these AIDS home test kits that we feel are very much unsafe at this point, and we definitely do not know its efficaciousness.

[Dr. Szapocznik's statement, with attachments, may be found in the appendix.]

Chairman WYDEN. Thank you very much.

Dr. Rundell, we appreciate your patience. Let me just again try to ask our witnesses to stay within 5 minutes. We will make a copy of your prepared remarks a part of the record in their entirety. Dr. Rundell.

TESTIMONY OF DR. JAMES RUNDELL, ASSISTANT PROFESSOR OF PSYCHIATRY, UNIFORMED SERVICES UNIVERSITY OF THE HEALTH SCIENCES, F. EDWARD HEBERT SCHOOL OF MEDICINE

Dr. RUNDELL. Good morning, Mr. Chairman. I should be able to stay under 5 minutes with no trouble. I am Major James Rundell, and am an assistant professor of psychiatry at the Uniformed Services University of the Health Sciences School of Medicine in Bethesda, MD.

I want to thank you for the opportunity to testify today on the subject of the FDA's consideration of licensing home test kits. I hope that my comments will shed some additional light on the issues being discussed today.

All military personnel are periodically tested for evidence of infection of the human immunodeficiency virus or HIV, and upon being found sero positive, individuals are immediately referred to one of the military's designated medical evaluation centers for a comprehensive medical evaluation.

Face-to-face counseling and education are included in this evaluation. They receive regular and continuing medical followup from that point on. In the Air Force, all sero positive persons are referred to Wilford Hall, U.S. Air Force Medical Center in San Antonio, TX.

The department of psychiatry there has been studying the emotional impact of knowledge of sero positivity. I would like to tell you some of the preliminary findings from those studies that have a bearing on the issue of home test kits.

Most HIV positive persons in the Air Force's mandatory testing program adjust well. However, significant adjustment problems do occur in many cases. For example, 2 in 10 patients experience anxiety or a depressed mood to the degree that causes some disruption in social or occupational functioning. Another 1 in 10 HIV sero positive patients will require treatment for clinical depression frequently with antidepressant medications. Alcohol abuse occurs in at least 1 in 10, and we believe probably more.

Various psychiatric grading scales reveal abnormally high levels of anxiety, depressed mood, or general distress in one third of the HIV positive patients. Suicides and suicide attempts are potential negative outcomes of a home testing program. Suicide rates in civilians with full-blown AIDS are up to 66 times that of the general population and 36 times that of individuals who are of the same gender and age.

Our experience with patients at early stages of HIV infection has been of the same magnitude. We have documented a suicide attempt rate at least 40 times higher than that of the Air Force in general. One patient in five admits to at least considering suicide as an option over the next year.

Attempts to decrease suicide and suicide attempt rates involve identification of risk factors in the population of concern. We have documented six factors that distinguish suicidal HIV positive persons from demographically similar nonsuicidal HIV positive persons. One, social isolation; two, multiple stresses other than HIV infection; three, denial of symptoms; four, evidence of disease progression; five, alcohol abuse; and six, high levels of anxiety and depression.

These suicide attempt risk factors are not unique to knowledge of HIV sero positivity but are frequently present. Interesting comparisons can be made between individuals who have just found out that they are HIV positive and individuals who have known for 1 year. There is only a modest difference in the frequency of psychiatric disorders and in measures of psychological distress between those two groups. Only the degree of depression appears to decline sig-

nificantly with time. The degree of suicidal ideation stays about the same.

We believe that not only should counseling accompany initial testing, but that followup counseling should also be available. To me, the debate is not whether to decrease the amount of counseling provided but how to increase both its availability and duration.

Certainly there is a difference between our population and individuals who might use the home test. Military personnel take the test because they are required to do so. However, no one knows who will take the home HIV test or for what reasons. One thing that we do know is that knowledge of HIV infection is accompanied by significant amounts of psychological distress, psychiatric disorders, and suicidal thoughts and behavior. This is in the setting of a very large military-wide effort to medically monitor all these individuals in a periodic face-to-face manner.

In summary, these findings support the reasoning behind guidelines established by multiple medical mental health and Government organizations. We find that we devote a large amount of both personnel and financial resources to help patients deal with the emotional consequences of knowledge of HIV infection. A sizable minority of this group of persons develop psychiatric disorders and require psychiatric treatment.

Once again, I thank the subcommittee for the opportunity to testify.

[Dr. Rundell's statement may be found in the appendix.]

Chairman WYDEN. Doctor, thank you very much.

One question that I have starting with you is that I gather that the military felt that it was important to do the research that you described because there was a concern that this research had not been done anywhere. Is that correct?

Dr. RUNDELL. Exactly. About 2 to 3 years ago when the military first started to do service-wide testing, and we began to look at what are the mental health complications of people who find out that they are sero positive, we had very little data to develop plans on. So, we decided to take a quick look and do a preliminary pilot study ourselves to see if we could get some basis on which to build a treatment program.

Chairman WYDEN. Your research identified what seemed to be a very significant rate of suicide attempts after people learned of their test results.

Could you project statistically what that might be on an annual basis?

Dr. RUNDELL. When suicide rates are measured in medicine, they are measured, and the measurement term is number of suicides or suicide attempts per 100,000 individuals in a population per year. The successful suicide rate in the Air Force runs about 11 per 100,000 per year. The number of actual suicides among HIV positive patients has been too low to calculate an actual suicide rate. However, we have had enough suicide attempts that we can calculate a meaningful suicide attempt rate. That number turns out to be about 4,535 per 100,000 per year.

Chairman WYDEN. Let me make sure that I got that. The suicide rate then would be 11 compared to 4,500?

Dr. RUNDELL. No, sir, not at all. The 11 is the actual completed suicide rate. The rate that I quoted, the 4,500 per 100,000 per year, is a rough estimate of suicide attempts. The usual ratio of attempts to successes runs between 7 and 20 to 1, usually around 10 to 1. So, the rate that I quoted you is probably something on the order of 40 times that of the Air Force in general.

Chairman WYDEN. That is what is important. So, in effect, you would project statistically 4,500 per 100,000 individuals?

Dr. RUNDELL. If there were 100,000 HIV positive individuals in the military.

Chairman WYDEN. Per year?

Dr. RUNDELL. That number of suicide attempts per year.

Chairman WYDEN. It would be something like 40 percent the suicide rate of the military in general?

Dr. RUNDELL. That is 40 times the suicide rate of the Air Force in general.

Chairman WYDEN. Tell us, if you would, what the experience has been with the military with respect to attitudes and sexual behaviors of military personnel who find out that they are HIV sero negative?

Dr. RUNDELL. If there is a readily available HIV test that is used by unprecedented numbers of low-risk individuals, there would be a large number of people who would suddenly experience knowing that they are HIV negative. It is not all clear that knowledge of HIV sero negativity facilitates safer sexual behavior. We have a number of anecdotes and reports that the opposite may be true, that it has not gotten me into trouble, so why change. Or I am not one of them, so I am not at risk.

Chairman WYDEN. What determines how an individual will react to the news that they are HIV sero positive?

Dr. RUNDELL. Well, the emotional reaction to the knowledge of HIV sero positivity depends on a number of factors. These include whether there is a preexisting psychiatric disorder, the quality of social supports, the amount of stigma perceived, and the biological effects of the virus on the brain.

The reaction to news of sero conversion is very much individualized and quite complex. Referral to mental health professionals is often made by counselors to help sort through these complex determinants that I have mentioned. One of the disadvantages that I can see in telephone counseling is that unless every community in the Nation has a local telephone counselor that there will not be knowledge of appropriate local referral resources that face-to-face counselors have available.

Chairman WYDEN. So, it is your view then, Doctor—the view of the military, given the fact that you are, in effect, the spearhead of this—that you cannot really envisage a telephone counseling sort of service?

Dr. RUNDELL. My personal views do not necessarily reflect the opinion of the Department of Defense, but I cannot think of many people who I have talked to who has disagreed with what I will say to answer your question. As I mentioned earlier, we do have evidence that knowledge of HIV infection carries with it emotional consequences that are sometimes severe, and when present are persistent.

To me the debate is not whether to decrease the amount of counseling or change it from face-to-face to telephone-based counseling, but how mental health resources can be more available for longer periods of time.

Chairman WYDEN. Your general view, though, is that telephone counseling is not all that it is cracked up to be?

Dr. RUNDELL. Well, in any mental health screening and evaluation in those instances where a counselor would refer a person to a mental health professional, and even counselors would probably tell you this, that in screening and evaluation that the examination of visual data such as general appearance, tearfulness, facial expressions, eye contact, posture, and grooming, are integral parts of the evaluation.

In additional, telephone counselors are geographically separated from the caller, and, at best, only a skeleton outline of a given community's resources can be provided.

Chairman WYDEN. We have a vote on the floor. But let me just ask you one other question, and then we are going to have to take a short break.

In your view, is telephone counseling for AIDS different than telephone counseling for other matters, other health matters?

Dr. RUNDELL. Absolutely; a lot of comparisons have been made to suicide hotlines, and most of the suicide hotlines that I am aware of are productions of local communities, not a toll free number that someone calls across the country. The person at the other end of that phone has a first-hand knowledge of local resources that they would refer these individuals to. It is also a management of last resort. We do not have any choice when we talk to telephone hotlines. With this, we do have a choice.

Chairman WYDEN. I would just like to ask the indulgence of this panel. There are a number of other questions that I would like to pursue with you. We have an important vote on the floor, and I will go and come right back.

[Recess.]

Chairman WYDEN. The subcommittee will come to order. I want to apologize to all of our witnesses for the bedlam that has required that we conduct this hearing in this fashion.

Dr. Rundell, those were certainly very startling and alarming figures with respect to suicide in particular.

Over what period of time did you collect the suicide data?

Dr. RUNDELL. The suicide data was collected over a period of 1 year, and I am glad that you asked that question, because I might take an opportunity, if I can have 1 minute, to summarize those numbers again. I know that I threw out a lot of numbers, and I want to make sure that they are written and recorded correctly.

It is useful to divide the numbers that I have into actual suicides and suicide attempts. Among civilians who have full blown AIDS, actual suicide rates are up to 66 times that of the general population and something like 35 or 36 times that of people of the same gender and age.

In the Air Force, we have not had enough actual suicides to calculate a meaningful rate. As far as suicide attempts go, there are generally between 7 and 20 times as many attempts as there are successful suicides in a given population.

Our suicide attempt rate, although it is a rough and preliminary estimate, is something along the lines of 4,500 per 100,000 per year, which is probably something on the order of 35 to 45 times that of the Air Force at large. So, I hope that helps to separate those numbers out and make them a little more clear.

We have been doing the suicide attempt data collection since 1987, and we recently went back and looked at the records for 1988. Just a preliminary look at those records indicates that suicide attempt rate is persistent, that it is continuing to be at that level.

Incidentally, almost none of the suicide attempts occurred immediately after finding out of HIV sero positivity. Most occurred several months later. Long-term, face-to-face followup is the best way to approach this problem. A one-time telephone counseling at the time of notification may well occur during a period of relatively low suicide attempt risk. So, that speaks to our feeling that there is a need for a longer term followup.

Chairman WYDEN. Major, it is my understanding that it is the practice of the military never to tell patients that they tested positive in a screening test, is that correct?

Dr. RUNDELL. That is correct. The way that the notification is handled is that a person must have two ELISA's that are positive and a Western Blot, and individuals are not informed at all until the Western Blot is confirmed, and they are told in person at a medical facility.

Chairman WYDEN. I consider this an important point, because you have just said that it is the policy of the military not to tell someone after a screening test that they tested positive?

Dr. RUNDELL. Exactly.

Chairman WYDEN. But it is my understanding that is often done in the area of home test kits, and that is what would be done in that regard?

Dr. RUNDELL. That is my understanding, and one of the concerns that I personally have is that we have enough problems with people who get confirmatory tests, and we have some concerns about what would happen with people who just get the ELISA's, and they are false positive.

Chairman WYDEN. So, you would question the public policy that would have people learn just on the basis of a screening test whether they tested positive?

Dr. RUNDELL. Based on my own personal experience, yes, sir; I would.

Chairman WYDEN. Do you know of anyone who does do that at this point, who tells someone, say a physician, after a screening test alone?

Dr. RUNDELL. The standard of practice as I know it among the people that I know in the medical community is that if there is a positive test, say for cancer, if the pathology report comes back, you tell the people in person. That is the standard of practice among all of the people that I know. There may be exceptions to that, but that is what I believe is the clinical standard.

Chairman WYDEN. One moment here.

[Pause.]

Chairman WYDEN. Ms. McGuire, you raised the issue of testing and counseling service as a means of providing access to health care services for persons with HIV infection.

Could you tell us how home testing would affect this kind of approach?

Ms. MCGUIRE. In the testimony I noted, Representative Wyden, and I know because of the other health-related work that you have done on the committee that you would understand, the importance of having the opportunity when an individual is in a health-related site to talk to them about care options, to talk to them about the systems that they would have to go through, and maybe to even link them up to those systems.

We see the counseling opportunities providing a unique opportunity to, in fact, have captive, if you will, for a few minutes a person who may not otherwise be linked to traditional and to public systems of care that could be very important to them in the time after they find out about their sero positive status.

So, as we try to build bridges, particularly in the poverty community in terms of health care access, the counseling opportunity that we have with HIV testing is a very, very important bridge that obviously would not be there in the context of whatever telephone counseling we would be providing in the course of home-base testing. Certainly, in the self-screening test, there would be no linkage at all.

So, the concerns that were expressed earlier about knowledge about community-based providers and about the systems, in many of the sites, in fact, the site that you are going to hear about later on today, the Whitman-Walker Clinic, you have counselors who then carry the individual through the process of applying for their benefits and the access to those services.

Chairman WYDEN. Just one question, if I might, Doctor Szapocznik. One of the strategies that public health officials are concerned about is that infected people should counsel their own sexual partners in order to get information about AIDS risk reduction.

Is there any evidence yet on how home test kits would affect this important aspect of public health policy?

Dr. SZAPOCZNIK. Well, actually, there is very little evidence on home test kits altogether. But in terms of extrapolating from what we know, the whole area of informing sexual partners is a very complex area. Disclosure to sexual partners is something that we handle quite intensively in our counseling programs, and it is something that requires ongoing work, because not everyone has a steady sexual partner at the time when they are tested.

So, in our case for example, we work with these individuals over a very long period of time. Each time a sexual partner comes up and each time a new relationship develops, the whole issue of how to go about telling my sexual partner that I am positive and how to handle safe sex in new situations has to be handled all over again.

Chairman WYDEN. I would have more questions if we were not so far behind in terms of our schedule. I want to thank all of you for your cooperation. I would also state again that we are going to keep the record open for additional comments and additional viewpoints. Thank you very much for your patience and your cooperation.

Our next panel is Dr. Peter Hawley, M.D., Whitman-Walker Clinic, Washington, DC, and Dr. J. Mehlsen Joseph, Ph.d, the American Public Health Association and the Association of State and Territorial Public Health Directors of Washington. If both of you could come forward.

Thank you both very much for your patience. At this point, if we are to finish, I am going to have to adhere rigorously to the 5-minute rule. I think you gentlemen have seen the procedures that we follow in our subcommittee.

Do either of you have any objection to being sworn as a witness today?

Dr. HAWLEY. No.

Dr. JOSEPH. No.

[Witnesses sworn.]

Chairman WYDEN. Also, we will insert for the record the statement of Jeffrey Levi, executive director, National Gay and Lesbian Task Force, Washington, DC.

[Mr. Levi's statement may be found in the appendix.]

Chairman WYDEN. We will make a copy of your prepared remarks a part of the hearing record in their entirety. We appreciate you summarizing your views today. We will begin with you, Dr. Hawley.

TESTIMONY OF DR. PETER HAWLEY, MEDICAL AND LABORATORY DIRECTOR, ON BEHALF OF WHITMAN-WALKER CLINIC AND AIDS ACTION COUNCIL

Dr. HAWLEY. Thank you, Mr. Chairman. I will reserve the issues in my prepared remarks concerning the accuracy of the antibody testing and the home situation and the value or lack of value of telephone counseling in order to spend some time talking about the community-based organizations and AIDS.

I am a physician and a board certified pathologist. Currently, I am the medical director and laboratory director of the Whitman-Walker Clinic. Whitman-Walker Clinic is the largest AIDS service organization of the Washington, DC, metropolitan area. Before working at Whitman-Walker, I served for 9 years as director of microbiology and immunology at the Washington, DC, Veterans Administration medical center.

I am here today to address concerns about so-called home testing for antibodies to the human immunodeficiency virus or HIV. I will speak both as a pathologist who has many years experience running immunology tests as well as the medical director of a community-based organization which has done HIV testing since the FDA licensed the ELISA in 1985. I am also representing the interests of the AIDS Action Council, the national policy arm of AIDS service organizations around the country.

I will address standard testing protocols, the counseling and educational needs of those who seek the HIV test, as well as describe the resources which community-based organizations can offer.

Like many other community-based organizations across the country, Whitman-Walker provides anonymous HIV testing. In 1988, we tested 4,227 people for antibodies to the HIV virus. People who want to take advantage of our anonymous testing program make

an appointment by giving us a code number. The client then comes in and receives pretest counseling which takes about 45 minutes and includes information on the meaning of the HIV antibody test for both negative and positive results.

We also offer HIV risk-reduction counseling including information on safer sexual practices, condom use, and information on the proper use of needles. Clients are provided ample opportunity to ask questions about HIV transmission and are encouraged to do so. The ELISA and the Western Blot confirmatory tests are fully explained so that the client can understand these tests. After blood is drawn, the client returns in a few days for results. These services, by the way, are provided without cost to the client.

Our experience demonstrates that the time period between drawing blood and receiving the test results is a very stressful one for many people. In fact, during the past 2 years we have known of at least four suicide attempts during this period.

When people do return for results, these are given on a one-to-one basis with a trained counselor. Counselors go through an extended training program during which they learn to recognize serious emotional reactions. Reactions have varied from very mild stress to very severe psychotic episodes. On at least two occasions, clients have been hospitalized directly after hearing their antibody test results in order to prevent them from committing suicide. In order to meet this considerable support need, Whitman-Walker Clinic employs 3 counselors in this program and has a volunteer group of 75 counselors.

We have learned over the past several years that routine counseling that occurs during the testing process is adequate for many people but certainly not all. Many will go on to require further counseling in order to adapt to the knowledge of the positive test or to learn and sustain behavior changes whether or not they are positive.

Like many other community-based organizations across the country, Whitman-Walker has developed a variety of individual and group support mechanisms for people who have had positive HIV antibody tests. Group sessions are scheduled on a drop-in basis. Usually these meetings attract about 15 people. Many people may attend these sessions for several weeks in order to talk over with others the experience of testing HIV positive. In addition, we provide drop-in counseling for those who wish to speak to a counselor one on one.

Whitman-Walker also runs a variety of support groups of HIV positive people, many of whom are presently without significance symptoms, or AIDS, or ARC. These groups run for 15 weeks and average about 10 people per group. Presently, at least two of these support groups are exclusively for women. All of our HIV positive clients are offered a referral to our HIV Medical Clinic, which can provide them with an evaluation for the presence or absence of signs and symptoms of HIV disease. Counseling related to medical issues is given as an integral part of this service.

For those with AIDS or with symptoms of HIV disease, our service programs include social workers, entitlements people, legal expert counseling, and support people. We have an extensive buddy system and an emotional support system as well as running several

houses with people with AIDS, and we recently opened a 24-hour nursing facility.

In spite of these various counseling opportunities, some people require much more intensive interventions. Thus, the clinic recently added to its staff two full-time counselors who at the present time each give 40 to 50 private counseling sessions per month to those people who are having trouble adjusting to a HIV positive result. Although these counseling experiences may last for as long as 8 separate hour-long sessions, many still require ongoing support. These individuals are referred to a network of psychologists and psychiatrists who have been identified by Whitman-Walker as being both sensitive and knowledgeable about HIV-related issues.

We have been repeatedly reminded of the devastating efforts of antibody testing on people's lives. Many equate a positive test with a death sentence. Hours of counseling may be required in order to convince healthy people that they, in fact, are in no immediate danger of dying. We estimate that of the average of 50 new HIV positive clients per month, 75 percent return to Whitman-Walker for medical evaluation and counseling, and at least 50 percent of those require further support counseling beyond the initial posttest session.

I do not wish you to construe anything that I have said or would suggest about home testing that I am against HIV antibody testing. It is quite the contrary. I am a director of a program which last year, as I said, tested well over 4,000 people and is likely to test even more this year. In addition, I thoroughly believe that with proper education that people do learn to make significant changes in their behavior to decrease their risk of HIV infection for themselves or decrease the potential of infecting others.

But HIV testing without accurate, sensitive, and knowledgeable counseling, and without absolute confidentiality guarantees is dangerous. We, as a society, need to make HIV testing and counseling more readily available to those who would seek it, particularly those who are at any risk of being infected with the HIV virus.

Unfortunately, home testing will not acceptably solve this problem, but will provide a profit for those who would capitalize on the pain and fear of HIV infection. Thank you.

[Dr. Hawley's statement may be found in the appendix.]

Chairman WYDEN. Doctor, thank you.

Dr. Joseph.

TESTIMONY OF J. MEHSEN JOSEPH, PH.D, DIRECTOR, COMMUNITY HEALTH SURVEILLANCE AND LABORATORIES ADMINISTRATION, MARYLAND STATE DEPARTMENT OF HEALTH AND MENTAL HYGIENE, AND PRESIDENT, ASSOCIATION OF STATE AND TERRITORIAL PUBLIC HEALTH LABORATORY DIRECTORS

Dr. JOSEPH. Mr. Chairman and members of the subcommittee, I am the director of Community Health Surveillance and the Laboratories Administration in the Maryland State Department of Health and Mental Hygiene. I appear before you today as president of the Association of State and Territorial Public Health Laboratory Directors and also to represent the American Public Health Association on the issue of home test kits.

Both organizations have great concern about the possible relaxation of the FDA's position on the approval of home test kits designed for self-diagnosis of infectious and communicable diseases. I know that there are simple rabbit kits that are available for use in a medical or health care setting for a variety of communicable diseases, and recently, one provided a license by the FDA for the HIV virus antibody test. We are concerned that it is only a matter of time that commercial organizations may attempt to convince the FDA that approval of this kit serves a public need.

We have strong reservations regarding the approval of such a diagnostic test kit, home test kit. Mainly, diagnosis and management of an infectious disease requires a comprehensive approach in order to rule out noninfectious causes which may be cancer and other bases and also clinical acumen to override test results that do not conform to clinical judgment.

It has been stated that when a physician makes a diagnosis of disease that 70 percent is based on the medical history, 20 percent is based on the physical examination, and 10 percent on laboratory tests. Basically, the information gathered from the medical history and from physical examination usually determines the tests that the physician may require.

The home test diagnostic kit, the whole procedure really reverses this process of diagnosis. It ignores the 90 percent of the diagnostic process, and placing the kits in the hands of a consumer will render a vast group of individuals unavailable for such physician scrutiny.

Both organizations that I represent oppose the approval of any type of home test kit for self-diagnosis for a communicable or infectious disease. Our concern is that self-diagnosis of a communicable disease may lead to inadequate and inappropriate self-treatment, certainly with certain sexually transmitted diseases and drug resistant strains spreading through a community without the knowledge or the awareness of public health officials, and certainly could thwart the prevention efforts of public health.

Also, self-testing would bypass mandatory reporting requirements that we have for certain diseases, communicable diseases, where the medical profession and the medical laboratory must report to health authorities, and this certainly could impede public health control measures to prevent the spread of communicable diseases and primarily sexually transmitted diseases.

Also, our concern of self-testing is that the individual is expected to be an expert to perform the test with proficiency the first time. We know from laboratory testing that it is not possible to be proficient the first time and unlikely the second or the third time that the individual attempts the testing. This lack of skill coupled with inappropriate and incorrect use of the tests could lead to an incorrect interpretation and some serious consequences as a result.

The real concern is the home test kit for HIV. Self-testing here would eliminate the opportunity of pre- and posttest counseling and the interpretation of test results by a qualified health care professional. Certainly, in the case of a positive test for HIV, it could lead a person to adopt life threatening and self-destructive behavior.

We strongly believe that it would be a great disservice to public health to allow the licensure of a home test kit for HIV. It is a test that really is not simple to perform, and it requires an experienced person to perform the test and properly interpret it. Even in the hands of a trained laboratorian in a regulated medical laboratory, it can require quite a bit of time to get proficient with that test.

It has been tried in our laboratory by professionals who have been doing HIV testing and have done well over 100,000, and it has been tested in a second State laboratory, and we have pretty much the same experience. It takes us approximately a week of testing to really get proficient with it. In the early days of testing, approximately 20 percent were false positive results.

It does take an experienced person to perform this test, so, it is unreasonable to expect a lay person to take this home test kit and perform it accurately the first time, the second time, or third time that they do it. Studies also reveal that false positive and false negative test results occur not infrequently with this test, very much as occurs with EIA testing. So, no screening test for HIV, and especially which is positive, has any validity until it is confirmed by the more complex confirmatory type testing.

We have great concerns about the inaccuracy of results from this test procedure. Certainly a false negative test would convey a false sense of not being infected when the individual is harboring the AIDS virus and spreading it unwittingly. A false positive test could result in serious emotional and psychological problems leading to self-destructive type behavior as I mentioned.

We believe that HIV testing without appropriate counseling and education serves no useful public health purpose. Testing could greatly compromise the opportunity for health professionals to offer the testing in conjunction with counseling and education which would provide the maximum public health benefit from such testing.

Neither the blood test collection kit for home use nor the home test self-testing type kit for HIV antibody would serve the public health need. In fact, they could hamper, and probably would hamper, current programs initiated by State and local health departments across the United States to provide free counseling and testing, anonymous testing, to deal with high-risk behavior modification, partner notification, and other public health measures which might be helpful to contain the spread of infection.

Surely, the quality of service would deteriorate and the delivery of health care would be impeded by the widespread use of the home test kit for HIV. For these reasons, the Association of State and Territorial Public Health Directors and the American Public Health Association opposes the approval of this type of home test kit.

Thank you, Mr. Chairman.

[Dr. Joseph's statement, with attachments, may be found in the appendix.]

Chairman WYDEN. Thank you both very much. I have a couple of questions.

Dr. Hawley, if I could begin with you. One of the arguments for home testing is that those who advocate it argue that people do not always go back to get the results of their tests, and I gather that

Mr. Millenson, who will testify later, has presented the subcommittee with an estimate that about 25 percent of those tested at AIDS clinics do not go back for their results.

What is the experience at Whitman-Walker?

Dr. HAWLEY. Our experience has been a good deal better than that. Last year, we had 90 percent of the people who were tested actually return to get their test results. Sometimes we know that people do not return at that particular time. We have anonymous programs, and the test results are not kept for long periods of time, and that many of those 10 percent who do not come back immediately will come back later on to be tested and do get their test results.

Chairman WYDEN. Is it your opinion, on the basis of having worked with many in the community, that it is difficult for people to take adequate blood specimens for themselves?

Dr. HAWLEY. The taking of a blood specimen at home is fraught with some problems. Even though it can be done fairly simply, one has to worry about whether the site from which the blood is going to be collected, which often would be the finger tip, had been properly washed, and that it would not have substances on it that could inactivate or change the results of the test.

We also worry about what happens to that sample in transportation. I realize that blood is transported all of the time, and we also at Whitman-Walker back and forth to our reference laboratories, but those kind of transportations are done with a great deal of care to keeping proper temperature, et cetera. When samples are going to be sent through the routine mail, there is always the problem of high temperatures or low temperatures, all of which can change the result of a test and make it less accurate.

Chairman WYDEN. One question for you, Dr. Joseph. One of the things that is so striking about the previous testimony that we heard from Dr. Rundell, is how little hard data has been available about some of these important issues like how people react when they are told a test result.

Is your association, the Association of State and Territorial Public Health Laboratory Directors, concerned that if there is testing outside of medical clinics and other places where there are professionals that it would be even more difficult to get information about who is getting AIDS, and how trends may be changing, and what the causes of the changes are?

Dr. JOSEPH. I think that is one of our important concerns, because even now there is difficulty obtaining information, even the way that testing is occurring now. We think that it would even be a greater difficulty with a self-test home test kit.

Chairman WYDEN. The only other question I have is for both of you. I also was very concerned about the remarks that Dr. Young made with respect to health care fraud, and particularly what he said in terms of AIDS and those who are concerned about getting the virus.

Are your organizations concerned about a growing number of exploitive kinds of efforts to take advantage of vulnerable people and, in effect, play to their fears?

Dr. HAWLEY. Very much so. We see people who will, in the field of laboratory diagnosis, spend sometimes incredible amounts of

money for a laboratory that does not cost more than \$2 or \$3 to actually run, and also people who will purchase medications at an incredibly high price, one example being some herbal therapies, and probably there is less than a dollar's worth of herbs in that group, and people are paying up to \$5,000 for that kind of therapy. So, of course, it is an incredible concern to us.

Chairman WYDEN. Dr. Joseph.

Dr. JOSEPH. Our association is primarily concerned with the fact of not just AIDS but with all self-diagnosis of communicable diseases, and that they may attempt to use medicines that they have at home or, on the black market, obtained the treatment that is certainly not effective treatment. So, there is a great opportunity for fraudulent practices there. We have that concern.

Chairman WYDEN. Just one other question.

Are you concerned that the people who are being targeted for home testing, those who are most fearful of disclosure, might essentially be those who most need face-to-face counseling?

Dr. HAWLEY. Of course we have no data to prove that, but instinctively one would gather that is probably true. Those people who, in fact, need both the support and information given during counseling are exactly the ones who would want to take advantage of home testing.

Chairman WYDEN. Dr. Joseph, did you want to comment?

Dr. JOSEPH. Yes; I would respond to that. I think that our concern is that the commercial forces are going to create a market beyond that particular group. I think that we see the same thing with a noninfectious disease type screening with cholesterol that is way ahead of any regulation or any recommendation naturally. So, I think that commercial forces are going to create a major market.

Chairman WYDEN. Unless you gentlemen have anything else that you would like to add, I think that I am going to excuse you in the interest of time.

Dr. HAWLEY. Thank you.

Dr. JOSEPH. Thank you, sir.

Chairman WYDEN. I think at this point that I would like to bring up Mr. Vincent R. Valles, president of International Medical Technologies, Palm Beach Gardens, FL.

Mr. VALLES. Good afternoon, Mr. Chairman.

Chairman WYDEN. Mr. Valles, thank you, and I appreciate your patience.

Do you have any objection to being sworn?

Mr. VALLES. Not at all, sir.

Chairman WYDEN. Please rise and raise your right hand.

[Witness sworn.]

Chairman WYDEN. We welcome you to our subcommittee. I am going to make your prepared remarks a part of the hearing record in their entirety. We will really have to stick to the 5-minute rule in terms of your testimony.

**TESTIMONY OF VINCENT R. VALLES, SR., PRESIDENT,
INTERNATIONAL MEDICAL TECHNOLOGIES, INC. [IMT]**

Mr. VALLES. Certainly. I will go right to the meat of thing, if I may. Our company is involved in two areas. One in establishing

and filing with the FDA to obtain approval for its tri-atomic oxygen generator for the purification of blood and blood products. In addition to that, our company, IMT Medical Centers, was established to provide HIV testing, consultation, and treatment of individuals who have proven to be HIV positive.

During our research, it became apparent to the management of the company that an opportunity existed for providing facilities to test for the HIV virus in a confidential setting. It appeared that the emphasis in the past, both medically and politically, was on those individuals who have progressed to the full blown AIDS.

There are indications that early detection of the virus and consultation regarding behavior, nutrition, and attitude changes should be the focus of the company's attention. During this period, we surveyed HIV positive individuals, individuals who are in the ARC stage, AIDS patients, local and national support groups, and the surveys produced the following results. HIV positive individuals fell into three groups, those who felt there was no hope for them, and were waiting to die, and were doing nothing, those individuals who were HIV positive who continued their life styles with disregard for others, and those who were under the care of a physician.

ARC patients fell into two groups. Those who were extremely well informed and searching for an answer, and those seeking alternate treatment modalities.

AIDS patients fell into three groups—subscribing to traditional treatment and primarily AZT, seeking alternate unapproved treatments, and seeking treatments in foreign countries.

It was determined by management that our services should focus on those individuals who are at risk, who proved to be HIV positive, and who are in the early stages of ARC. The following represents the at-risk groups: Single individuals with multiple partners, individuals considering marriage or entering into a long-term relationship wanting to be assured that they were not jeopardizing the other party, individuals in the high-risk groups who concluded that they needed to know, individuals concerned as a result of a blood transfusion, and individuals working in medical facilities.

The Cambridge BioScience. We first became aware of the quick test in an article in the November issue of U.S. News and World Report. The Pandex Division of Baxter Healthcare Corp., the marketing company for the quick test, responded to our inquiry. They were cautious in allowing us access to their product. Pandex personnel were extremely helpful in instructing us on the proper use and in evaluating the results.

Our protocol is as follows: The attending physician conducts pre-testing counseling. A registered nurse trained in this testing process administers the test. We find that if the test proves positive, that a second test is performed. If both tests are positive, the patient is informed that the test is inconclusive and a Western Blot test is performed by an outside laboratory. This patient is not charged for the second test or the Western Blot. The attending physician conducts posttest counseling.

We believe that being able to provide a quick screening test is important to the public. Patients testing negative for antibodies to HIV express relief and appreciation for not having to wait for up

to 2 weeks for the results. We believe that the quick test has been instrumental in encouraging people to be voluntarily tested.

The State and Federal regulations. As we have just opened our business, we have not experienced any difficulties on a State and Federal level. We have found that we do need licensing as a laboratory, and we are in the process of preparing to file for that licensing.

It is my opinion that Americans do not yet understanding the consequences of the HIV epidemic. It has begun to enter the general population. This will bring it close to every household in America. This is happening, and we must address, as a nation, the following issues: We must develop medical capabilities and facilities to meet this problem. We must provide private and public funding to address the added case load. We must develop facilities to test the estimated 40 million people needed to be tested now.

Whenever conditions such as these face a Nation, it brings out the best and worst in Americans. We believe that it is imperative that proper training and regulations be enacted, and that these are required to ensure that the American people receive the very best testing, treatment, and counseling in the fight against HIV/AIDS. It has become more apparent that we need to devote as much energy and resources to the source [HIV] as we are to the results [AIDS] of the problem.

[Mr. Valles' statement may be found in the appendix.]

Chairman WYDEN. Mr. Valles, thank you. I noted in your testimony that you said that we have not experienced any difficulties on a State or a Federal basis. But we were sent a copy of this letter from Connie Charon, director of the Office of Licensure and Certification, dated today.

Have you seen that?

Mr. VALLES. No; if it is dated today. Is it dated today?

Chairman WYDEN. Yes.

Mr. VALLES. Well, I am here.

Chairman WYDEN [reading]:

It has come to the attention of this office that International Medical Technologies is operating a clinical laboratory without a valid current license pursuant to chapter 483, part 1 of the Florida statutes. This activity is in direct violation of section 483.091 Florida statute. The laboratory is also in violation of S.381.6094(c) which states that all tests performed for HIV virus shall be performed in a laboratory licensed under the provisions of chapter 483 Florida statutes.

According to an advertisement in the News Sun Sentinel, February 15, 1989, the IMT Medical Center is offering HIV tests to the general public. This was confirmed in an onsite investigation by Mr. Joe Barloletto, Mr. Bob Scott of the Department of Health and Rehabilitative Services in Palm Beach County on March 6, 1989.

This is to advise that you are to cease and desist immediate operation of the clinical laboratory known as IMT Medical Center in Palm Beach Gardens.

Chairman WYDEN. And then it goes on.

What comment have you to that?

Mr. VALLES. Certainly, if we have been in violation, it was due to a lack of knowledge. We will comply and do whatever is necessary to comply to that. Both of those individuals, Bob Scott, and the other individual were in my office. We have not heard from them from that day. If you presently possess a letter in your hand, I have not received it. I was up here yesterday.

I have already been informed at this particular meeting that we were in violation, and I can assure you that when I leave here that we will stop until such time as we get the appropriate license.

Chairman WYDEN. Why did you say in your testimony that, "We have not experienced any difficulties on a State or a Federal level"?

Mr. VALLES. Well, it is very simple. If you received the letter today, and I am here, I do not know anything about. So, how can I pose a problem. As I said before, to date we have not had any correspondence with the individuals who were in our office.

Chairman WYDEN. What kinds of questions did the State ask when they were there to visit you earlier? I gather, as you said, that they came to visit you earlier.

Mr. VALLES. They wanted to look around the facility and go through the procedure that we go through. We provided them with our posttest counseling questions and pretest questions, and I showed them the test. We only conduct a test when a doctor is there, and the doctor does the consultation. At that particular time, the doctor was not there. So, primarily, that is basically it. We supplied them with the information from Cambridge BioScience, and I have not heard from them.

Chairman WYDEN. Are you of the view that you are in compliance with Florida law?

Mr. VALLES. I am sorry?

Chairman WYDEN. Are you of the view that your company is in compliance with Florida law?

Mr. VALLES. Based on my conversation just about 20 minutes ago, I would say no.

Chairman WYDEN. That you are not in compliance?

Mr. VALLES. That is correct.

Chairman WYDEN. And you will cease and desist until you get in compliance?

Mr. VALLES. It is my understanding that we have to cease with the BioScience test, but we can still do blood tests with an outside lab. That is the information that I received.

Chairman WYDEN. You are ahead of me on that one.

Mr. VALLES. OK.

Chairman WYDEN. With respect to this matter of the physician, my understanding is that you have a physician 1 day a week?

Mr. VALLES. That is correct.

Chairman WYDEN. What happens on the other days?

Mr. VALLES. That is the only day that we schedule tests.

Chairman WYDEN. Oh, I see.

Mr. VALLES. I think that we made that clear to your representatives when they were here to visit us.

Chairman WYDEN. So, the physician is there at the only time when you conduct these tests?

Mr. VALLES. Yes.

Chairman WYDEN. One of the things that I noted—frankly you are going to have to take us through this. In a corporate overview text for the company, it states that the purposes for the treatment facility were, "To provide positive cash-flow to support the company's effort in obtaining FDA approval for the tri-atomic generator for the purification of blood and blood products."

Unless I am not reading this accurately, it appears that the reason that you are interested in AIDS testing is to generate some cash-flow for another company that, in effect, would market the ozone machine.

Am I reading that correctly?

Mr. VALLES. That was the purpose; yes.

Chairman WYDEN. OK.

Mr. VALLES. It has not turned out that way, but that was the purpose; yes.

Chairman WYDEN. But the principal point of the effort was not initially to get into AIDS testing, but, in effect, to generate cash for another part of the business?

Mr. VALLES. I believe that the result of providing that cash is the HIV testing. So, we primarily got into the Medical Center as a means of generating cash-flow. We chose HIV as we felt that there was a demand for it and a need.

Chairman WYDEN. Are you seeing a significant number of the people who are considered at risk, homosexuals and IV drug users? Who are you seeing?

Mr. VALLES. It is rather interesting. From what we can determine, 80 percent of the individuals who have come in for the test, which has been very limited by the way, have not been in a high-risk group. We have had women who have come in who had relations with an individual—I am just picking out certain ones here—who felt that they were suspect. We had a couple fly over from the Bahamas last week, a married couple, for testing.

Chairman WYDEN. Let me ask you about one of the ads that you ran in the Fort Lauderdale paper. It said, "HIV positive? Why wait? New quick test available, confidential, results in 5 minutes."

Now, what is that referring to, or have you all changed this since that ad came out?

Mr. VALLES. When the representatives came in from the State, that ad was running, and it was changed the following day. We eliminated the 5 minutes.

Chairman WYDEN. But they, in effect, told you that was not acceptable?

Mr. VALLES. No; they did not say that it was not acceptable. They felt that we ought to reconsider it, and we did.

Chairman WYDEN. But you are doing the 5-minute test?

Mr. VALLES. That is correct.

Chairman WYDEN. How did you get to the Cambridge BioScience test in the first place?

Mr. VALLES. We first saw the advertisements in U.S. News and World Report in November of last year, and, based on that, we contacted them concerning their test.

Chairman WYDEN. I think that it is their view that they are very concerned about who they sell to.

Your background, are you a physician?

Mr. VALLES. No; I am a backer.

Chairman WYDEN. There is a doctor 1 day a week?

Mr. VALLES. That is correct.

Chairman WYDEN. What is done in the rest of the 4 days?

Mr. VALLES. We run our business out of that particular facility.

Chairman WYDEN. OK. I think that unless you would like to add anything further that we will excuse you at this time, and thank you for your patience.

Mr. VALLES. Thank you, sir.

Chairman WYDEN. Our next witness will be Mr. Elliott J. Millenson, president, Cross Industry Management, Rockville, MD. Mr. Millenson, welcome.

If you do not mind, we can just keep you on your feet and go through the formalities. Do you have any objection to being sworn?

Mr. MILLENSON. No.

[Witness sworn.]

Chairman WYDEN. Mr. Millenson, thank you for your patience as well. We will make your prepared remarks a part of our hearing record in their entirety, and if you could summarize your views in 5 minutes, that would be very helpful.

TESTIMONY OF ELLIOTT J. MILLENSON, PRESIDENT, CROSS INDUSTRY MANAGEMENT

Mr. MILLENSON. I wish I could.

Chairman WYDEN. Well, we are going to have to adhere to the 5-minute rule.

Mr. MILLENSON. OK. Certainly.

I think it might be helpful if I have to be brief if I could demonstrate the product, particularly to distinguish this from the Cambridge BioScience product which was demonstrated earlier and is only intended for use in a health care environment.

That is a latex agglutination test. That sort of test is only pertinent to tests conducted by health care professionals.

The way this test would be used is as follows: Users would follow illustrated test instructions to obtain a blood specimen onto a piece of filter paper.

All right. Essentially, filter paper is an approved blood transport medium, the same as a test tube. This filter paper is made by a company called Schleicher & Schuell who are the only manufacturers of the paper, and it is the same paper that the CDC uses in their studies. It is also used by some insurance companies in commercial applications.

To use the test, the user would——

Chairman WYDEN. Mr. Millenson, if you could address the Chair.

Mr. MILLENSON [continuing]. To use the test, an individual would use this lancet to collect a blood specimen, and place a drop or so of blood into each of these two circles. I might add that we tested this in clinical trials with several hundred individuals as part of determining whether people could do just that. We determined that people could, in fact, collect the blood specimen. I might add for the subcommittee, in the testimony, that this has been proven in blood glucose monitoring kits.

When we looked at data from blood glucose kits, and those are FDA approved products, we decided that the data was not as pertinent to our product due to some differences. So, we conducted our own clinical trials and found that the instructions and the illustrations in the instructions were very important in terms of getting an adequate blood specimen.

In the course of clinical trials, we made several changes to the illustrations. That is, we made several changes to the way we instructed people to take the blood sample. I also might add that people had access, telephone access, and would when the test was marketed, to our counseling center, if they had any problems collecting a blood specimen.

After collecting the blood specimen, the individual tears off the top of the filter paper, which contains a unique code number known only to them. They then place the specimen paper and the lancet they used in collecting that specimen into this mailer. They place that in an envelope in an overnight letter—a Federal Express overnight letter—and send that back to our medical university laboratory for testing.

AIDS specimens in test tubes and on filter paper like this are routinely shipped around the country. However, understanding that some people have expressed a great deal of concern over problems with shipping, we decided for our test kit we would use Federal Express. This would also ensure, and no offense to the U.S. Government, this would also ensure that the test was received by our laboratory 1 day after it was shipped by the customer.

We met with the chairman of Federal express, Mr. Fred Smith. Following those meetings, his staff subjected our packaging to thorough tests. They consulted with medical consultants at the Center for Disease Control, and they gave us their commitment that they felt there was no safety hazard posed by this product.

Once it is received by our medical university laboratory, this test specimen is tested using the same procedure that the blood would be tested by a doctor, obtained by a doctor or hospital.

Obviously, it does not matter to a laboratory whether the blood was obtained by a doctor or the blood was obtained by someone putting the blood on this filter paper themselves. The only thing that is important is that there is an adequate blood sample to be tested.

Following that, the laboratory technicians test this using both the ELISA and Western Blot procedures. That is the ELISA, which is the screening test. A second ELISA is performed if the test is positive, and then a Western Blot confirmatory to confirm results.

Those results are then made available to our counseling center. One week after the test is taken, the individual calls into the counseling center, presents his unique code number, and receives test results and counseling by telephone.

The counseling center is staffed by social workers, psychologists, and physicians. When individuals call in and key in their code number, if their code number is a known positive result, then their call is directed automatically to a crisis intervention team that handles that call. If it is a negative result, it goes to counselors, the same sort of counselors that you would see in public health clinics.

That's it.

[Mr. Millenson's statement, with attachments, may be found in the appendix.]

Chairman WYDEN. Let me ask you a few questions. Generally about your enterprise and then some specific policy questions.

You first submitted your premarket application to the FDA during 1987. It was during March 1988 that the FDA rejected your application. Is that correct?

Mr. MILLENSON. That is not entirely accurate in terms of terms.

On December 30, 1987, we submitted a premarket approval application to the Food and Drug Administration. That is this sort of application, with hundreds of pages of data from our clinical trials and associated data, which answered concerns that the FDA has raised subsequently—concerns about shipping, the ability of people to adequately obtain blood specimens, problems of counseling, all issues addressed in our premarket approval application.

Under statute established by Congress, the FDA has 45 days to study an application to determine whether it is acceptable for filing.

By that, the FDA means does it have all the elements necessary to be accepted for review, much like a college might look at an applicant and say, are the high school grades in, recommendations, things like that. They do not evaluate whether that student should be accepted to the college, only whether the application is complete.

After 45 days, the FDA did not respond to our application, and only responded after the intervention of one of your colleagues, Congresswomen Connie Morella from Maryland, and responded to our application after 91 days saying it was not acceptable for filing. That is not an uncommon practice by the FDA. Oftentimes, the FDA does not accept an application for filing because it is incomplete.

What was unusual and has never happened in the history of the agency is that the reason they gave for not accepting our application was that it was for use within the home. They established guidelines for acceptance of applications and said that only tests which were used in a comprehensive medical environment where the specimen was collected by a medical professional would be accepted.

So, in other words, they not only did not accept our application, as a policy they established that they would not accept the applications from any company.

That is unprecedented. It is a violation of the FDA statute. But that is what they did.

Chairman WYDEN. I think right at the heart of your concern, and at the heart of your case, is your assertion that a significant number of people could get tested for AIDS only with a home test like the one that you developed.

Of course, we heard testimony previously to counter that from the people at the Walker-Whitman Clinic. But you cite a study that you did, or Universal Hospital Laboratories.

I know of no other studies that point to that. Are there any?

Mr. MILLENSON. Yes; if you look later in the testimony after the prepared remarks, you notice that there is another study cited.

Chairman WYDEN. Who did that?

Mr. MILLENSON. University of California at San Francisco.

Chairman WYDEN. What does that study say?

Mr. MILLENSON. What that study shows, and I would be happy to make that study available for the record, and I would also be

happy to answer questions that were raised, to respond to some of the issues that were raised previously by people concerning seroprevalence specificity and things like that.

The study, our study showed that 30 percent of people who want to get tested for AIDS would only get tested using a home test. The UC San Francisco study was conducted on over 500 bisexual men at high risk. It was a 2-year study. The methodology for that study was at the beginning of the study—this was conducted, the senior person I believe was Thomas Coates, who is codirector of the UC San Francisco Center for AIDS Prevention Studies—over a 2-year period they followed people who had expressed interest, who were at high risk, and had expressed some interest in taking an AIDS test.

What they found was that a significant percentage of individuals—I believe it was 60 percent and that is in the testimony, I have the study here—did not get tested for AIDS.

A frequently cited reason was fear of results.

Another frequently cited reason was fear that confidentiality of results would not be maintained.

Let me explode another myth, and I would also be happy to provide for the record studies—

Chairman WYDEN. Dr. Rundell said that there was no data available on this point. Is Dr. Rundell wrong?

Mr. MILLENSON. I think he is well-meaning, but I think he is misinformed.

Chairman WYDEN. Well, can you give us a copy of what you are quoting from there, from the University of San Francisco?

Mr. MILLENSON. Yes.

Chairman WYDEN. I think I will send the staff to get a copy of that, and I would like to see it.

Mr. MILLENSON. It should be cited on the back, in a later part of the testimony, anyway. Let me see if I have it with me.

Well, I know it looks like something that depletes ozone, but I do not have the study with me. It is cited in the extended remarks, and I can provide a copy to you.

Chairman WYDEN. We will hold the record open on that point. But I found very significant Dr. Rundell's statement. The military has had a very good program where he said there was not any data available.

Mr. MILLENSON. The military program is not a voluntary testing program.

Chairman WYDEN. The military program said there was a virtual total absence of any data in this regard.

Mr. MILLENSON. The military program, in the October—I do not know what the exact date is; they have that as well, I hope—issue of the New England Journal of Medicine, I believe it was October 13, reported on a study done on 135,000 military recruits. That study was talking to the issue of HIV prevalence.

What that study found was that the false positive rate—those terms have been tossed around in this debate—the false positive rate, meaning the number of people who are not positive for HIV infection but test positive, they found that rate was 1 in 135,000.

They concluded from that data that a screening program would be safe for quote, "low risk populations."

Chairman WYDEN. Is it not correct to say that you have said that there are many irresponsible people and companies trying to get into this field of home test kits?

Mr. MILLENSON. Yes; I have, and there are many irresponsible people in many fields.

Chairman WYDEN. I just want to have that on the record that you have said——

Mr. MILLENSON. Yes; and I think there have been a number of articles——

Chairman WYDEN. So, we are clear on that regard. You have said that there are many irresponsible people and companies that have applied to offer home test kits to the public.

Mr. MILLENSON. I am not aware that they have applied.

Chairman WYDEN. But you have said that.

Mr. MILLENSON. I have said that, and there have been articles in the press that have reported actions of companies, specifically actions like offering tests with only an ELISA test. Specific actions like offering a test with no counseling. Specific actions like offering these tests illegally, not just proposing to offer them. That, to me, Congressman, is irresponsible.

Chairman WYDEN. But you understand my concern here. When someone like yourself who seems to be concerned about the same consumer protection issues that I am—the question of training, counseling, and the like—says that there are many irresponsible people who are trying to offer these tests, that is what policy makers are concerned about, because we have to be able to have a system, particularly when there is a significant number, to protect the public.

Mr. MILLENSON. That is what the Food and Drug Administration is supposed to do. Unfortunately, in this matter, the FDA has not had an open mind. Most products, virtually all products except for this, product categories that is, they accept data from clinical trials. That is how they judge whether a company is responsible or irresponsible.

In this case, and it is unprecedented, the FDA has said we will not accept data. That is why I have disclosed our data from clinical trials, Congressman. The data that we collected was expensive to collect and very time consuming. No company discloses that data prior to product approval. We are the first I know of that has ever done that because the FDA will not accept our data.

Chairman WYDEN. On the counseling issue, you have repeatedly cited the suicide example. It is my view that the suicide example is altogether different because in a suicide situation you have no choice but to be on a telephone and doing everything possible.

Could you tell me for the record why you think that this is analogous? Because it seems to me very clear, and I felt Dr. Young said that as well, that face-to-face counseling is possible in most instances and that it is not at all analogous to suicide.

Mr. MILLENSON. Let me respond by making several points.

First of all, I am not a physician. I have a bachelor's degree from Cornell and a master's degree in business from Harvard Business School. I have worked in the public health field. In fact, the U.S. Public Health Service bestowed on me an award for contributions to the Government's smoking education program.

This product was developed by physicians and psychologists. People from UC San Francisco, people from Harvard University School of Public Health, people from Medical University of South Carolina, people from University of Denver, qualified physicians and psychologists, people who have studied the research. I can report on what they have said. I think that there may be differences of opinion among medical people, but let me address—

Chairman WYDEN. On the question of counseling over the phone, and whether suicide counseling is analogous to AIDS counseling?

Mr. MILLENSON. Let me make this point, Congressman. I would agree with you that it is preferable for people to have face-to-face counseling, in a perfect world. In a perfect world, people who were contemplating suicide should be able to talk to their physician. As you probably know, many people do not have a personal physician. The reason that suicide prevention centers were established under the Community Mental Health Services Act was to give a resource to people, a resource that we mention in our testimony is used, according to a 1977 study, 10 million times a year, so that, in a moment of crisis, if they cannot get to a physician, they can use a phone.

Chairman WYDEN. Why do we not sell home test kits only when they cannot get to a physician? You have repeatedly made the point that telephone counseling with respect to home test kits is like suicide counseling.

Mr. MILLENSON. No; I think you are misinterpreting my remarks. What I am saying, and I think we are in agreement, is many people are reluctant to get tested using current testing alternatives. They will not use them. Current testing alternatives are inadequate. People are afraid to go to their physician. Some people are not. Some people prefer that, and I believe that they should be able to go to their physician. This would not preclude that.

But for people who want to get tested and will not get tested, an AIDS home test is their only alternative, were it on the market.

I might add, from my testimony, once someone, an individual is infected with the HIV virus, a median time of 9.6 years has been established by researchers at UC San Francisco, just reported last week, between becoming affected and symptoms emerging. That is, for that period of time, there is no way other than a test to know whether you or your partner is infected.

Further, research studies have shown, and they were alluded to earlier, and I will also include those in the testimony, that significant percentage of individuals who find out that they are HIV-positive do not tell their partners.

Chairman WYDEN. What information do you have that indicates that anonymous AIDS testing is not readily available today?

Mr. MILLENSON. Well, Congressman, anonymous AIDS testing, the perception among individuals is that the current testing procedure is not anonymous. People have expressed a fear that someone would see them.

I would also point out to you, and I will include in the record from an October 13, 1988, issue of the Journal of the American Medical Association, an article which provides data—there are two articles in there. The first article discusses, from Cook County Hospital in Chicago, an incident where an individual went to a hospi-

tal for a blood test. Not an HIV test, a blood test. An HIV test was performed without informed consent, which is very common, and that sort of occurrence is included in other articles such as a January 8, 1988, issue of *Journal of the American Medical Association* from a study in Minnesota. That individual was tested without informed consent. His test results were sent to a clinic who notified his employer, and he subsequently lost his job.

So, this is in our current testing environment. Even when people feel they are not being tested, even people who do not want to be tested have their anonymity violated.

A home test is clearly an anonymous way to get tested, and, I think, given this crisis that we have, it is perplexing to me that we are concentrating not on overcoming obstacles but letting obstacles overcome us.

We are not concentrating on, let us see how this can be shipped properly. We are concentrating on, this could never be shipped properly.

Chairman WYDEN. Not over here at the Small Business Subcommittee on Regulation.

Mr. MILLENSON. I certainly know that.

Chairman WYDEN. Because we are interested in having those questions addressed. If people are properly trained, if there is proper counseling, if there is sensitivity to issues we are bringing up, we should go forward with every possible technology.

But let me just say something. Virtually everyone that has testified thus far today has taken exception with your views on the accuracy question, on the confidentiality question, on the counseling question.

I am going to follow up on this University of California study, because if that breaks some new ground, we are anxious to see it.

Dr. Young, Dr. Parkman from the Food and Drug Administration, Dr. Rundell certainly, are all three people who work in this field with some expertise, and some concentration, and they did not feel that there was any in our new data.

Mr. MILLENSON. Congressman, I can only address the fact that the new data, which is now old data, that we submitted to the Food and Drug Administration, has not been studied by that agency. The agency has expressed concern about shipping. If they are so concerned about shipping, Congressman, I would ask that you investigate why the CDC is allowed to ship this same paper through the mails when the Food and Drug Administration has such concern. I am not saying that there should be regulations so that we can ensure that an irresponsible company does not ship this irresponsibly.

But the fact of the matter is, shipping is not the concern. It can be done responsibly.

Test quality is not the concern. We know from CDC data, from data of the Johns Hopkins School of Public Health, and from our data from clinical trials where there was 100-percent concordance between samples taken on specimen paper and venepuncture samples.

So, that data may not be available to the Food and Drug Administration, and they may not be making their evaluations based on that.

Chairman WYDEN. How much of your data in your premarket application is based on your clinical trials as opposed to research conducted by others?

Mr. MILLENSEN. There is a good deal of data in our premarket application. We cite, I think, almost 60 cites, and I would include our cites for the record, if that would help the subcommittee. That also is unprecedented for a company to include so much information from a premarket approval application.

I might also mention we are no longer in the business. When the Food and Drug Administration is not willing to study our data and has stated as a policy they will not study our data or anyone else's, there is no reason to stay in this business.

Chairman WYDEN. But when you sent in your premarket application, how much of it was based on your clinical trials as opposed to research conducted by others?

Mr. MILLENSEN. That is a difficult question. It is the data—well, I will address it. It is on both. For example, in shipping, we studied shipping. We also used CDC and Johns Hopkins data.

In collection of specimens, we used our data because no data has been available on lay person collection of specimens. So, we had several hundred people participate in clinical trials.

On temperature testing—and one individual from Whitman-Walker Clinic talked about the adequacy of temperature controls. There is an abundant amount of data on that. We also tested that as well.

We compared all samples obtained on filter paper to venepuncture samples taken from individuals, and compared those.

But, I might also add, and you indicated that the Commissioner of the Food and Drug Administration had expressed concern about quality, perhaps I can accept that he has not studied our application, but there is abundant data from CDC, Johns Hopkins, that this is adequate as a collection medium. Just 2 weeks ago the Food and Drug Administration approved an ELISA test manufacture, the same one we used, as an approved ELISA test to be used with filter paper. Of course, the CDC uses the Western Blot as well.

Chairman WYDEN. Did you base your position on counseling on evidence that you developed or evidence developed by others?

Mr. MILLENSEN. That is a loaded question, Congressman. It would be difficult to—both. It is difficult to study counseling. In a clinic, as with our home test, an individual receives results, anonymously, and then vanishes. To do followup studies on that individual would be very difficult.

We base our evaluations on an abundant amount of research, on counseling, on telephone counseling. We found, for example, that the rate of followup, and I might also correct a misperception, the counseling we do on the telephone when a person receives his or her results is an initial counseling session. It is not the total counseling someone receives. Our counseling center would have available to it resources in the individual's community. It would also have the latest information on AIDS. Information which we have seen in the real world of AIDS testing is not always accurate. Physicians do not always know the difference between testing positive for an ELISA and testing positive for the Western Blot confirmatory.

So, the data suggest that the rate of followup, and there is abundant data which I have included in my testimony from the University of Denver where most studies have been done on telephone counseling—we had people on our advisory board from that university—that show that the rate of followup, when the first visit is over the phone, versus the rate of followup when the first visit is face to face, is significantly higher.

That is, more people seek additional treatment after a telephone counseling session. I might also point out that, from our research we discovered, that the quality of counseling—and I know you are very sensitive to this from the work you have done in studying in vitro fertilization clinics—the quality of health care, the quality of counseling, is not always adequate in the health care environment today.

A company which is responsible and is regulated would centralize the testing facilities so that it could be ensured that testing was high quality, that counseling was the highest quality possible and that—period.

Chairman WYDEN. One last one. I think it has been your view that there is a correlation between the results produced by test kits and tests done by doctors.

One of the things that physicians have told us is that they really are very different kinds of species, that persons reviewing mailed-in specimens, for example, generally have to operate with much less information. They do not have patient histories. They do not have other kinds of testing or specimen information which might be in someone's file or something of that nature.

How is that dealt with?

Mr. MILLENSON. That is generally true. But let me explain why it is generally true.

Chairman WYDEN. I think I know it is true, but how do you deal with it? It seems to me there is a virtual vacuum if you are getting it in the mail as opposed—

Mr. MILLENSON. We are not getting this—oh, receiving the test.

Chairman WYDEN. Yes; that is what I mean, rather than in a physician's office where there is a big, thick file, all based on the patient's history.

Mr. MILLENSON. The reason that physicians make a great deal of their diagnoses by seeing the patient and by talking to the patient is because various symptoms, for instance if you feel pain in your cheek or pain in your back, the differential diagnosis for that could be a whole range of diseases. Face-to-face discussion is required. I might add that 11 percent of pediatrics, according to the National Center for Health Statistics, is practiced over the phone.

The Commissioner is right in that, but he is wrong in that the HIV test does not require face-to-face consultation to determine whether an individual is indeed HIV positive or is negative. It is that simple. Our blood supply is tested, for example, by the American Red Cross, for the presence of HIV antibodies, without seeing the individuals who donated that blood. The blood is simply tested. If it is HIV positive, it is thrown out.

Chairman WYDEN. We have a vote on the floor. Let me just excuse you, unless you would like to add anything further. You have obviously spent a great deal of time and money in developing

what you clearly believe to be an important AIDS testing alternative. We are certainly going to indicate to the FDA at the end of this hearing that a very careful and very thorough examination of what you presented be considered, along with the testimony of the other businesspersons and entrepreneurs who have come before us.

Thank you for your patience. We will leave the record open so that you and others can add your views. With some patience from our last witnesses, I will go and make this vote very quickly and will come back and hear from Dr. Johns and Dr. Berns.

[Recess.]

Chairman WYDEN. Again, my apologies to our witnesses. Dr. Patricia Johns, Ph.D., Department of Laboratory Licensure, State of Florida, Tallahassee, FL, and Dr. Donald Berns, Center for Laboratories and Research, New York State Department of Health, Albany, NY.

You have been very, very patient, have outlasted virtually everyone, as I look around, and we thank you for that patience.

We do swear all our witnesses. Do either of you have any objections to being sworn today?

[Witnesses sworn.]

Chairman WYDEN. Thank you both. Dr. Berns, I know that you are on a very tight schedule. Why don't you proceed in a fashion that you have time for, at this point, and we will make your prepared remarks part of the hearing record in their entirety.

TESTIMONY OF DR. DONALD BERNs, NEW YORK STATE DEPARTMENT OF HEALTH, WADSWORTH CENTER FOR LABORATORIES AND RESEARCH

Dr. BERNs. Thank you, Mr. Chairman. What I would like to do is a little bit unusual. I would like to direct some remarks in addition to what I have submitted, which reflect on the testimony of the last speaker, Mr. Millenson.

I think there is some misinformation, if we consider what was presented as a home test kit. That is not a home test kit as submitted. That is a device for submitting a specimen to be tested at a clinical laboratory. As such, in the New York State situation, that would not be permissible because the specimen would not be submitted by a physician, and the laboratory would have to be a laboratory duly licensed in New York State. I would like to distinguish that device from a home testing kit. That is the first thing.

The other thing is, I would also like to, for the record, clarify the comment about the Defense Department testing in low-prevalence groups. I think it is very important that we understand that the experience of the Department of Defense in HIV testing is unique. It is the largest program for screening specifically low-risk populations, and it has amply demonstrated the need for a single source for all confirmatory HIV testing with a single, demonstrable standard for HIV positivity.

It has been repeatedly demonstrated that the Western Blot procedure and its interpretation requires continual monitoring and is subject to shortcomings in both technique and interpretation. The Defense Department program only functions as well as it does with a single laboratory performing Western Blots as a consequence of

frequent blind specimen challenges and inspection of the interpretation of all positive Western Blots. Such a process is not achievable in programs in which decentralized confirmatory testing can occur.

Then I would just like to move and not discuss the New York State program for dealing with mobile laboratories. That is in the remarks that I have submitted for the record. I would just like to confront the situation with home testing kits as such.

It is a problem which is quite different. The problem of home testing kits, such as those proposed to detect the HIV virus, is much more vexing since current and foreseeable State regulations will not hold the public harmless from the introduction of such testing.

The HIV antibody screening test which is based upon ELISA or latex agglutination technology is an example of the finest technological accomplishments of the biomedical technology revolution. This technique and related techniques have been applied to faster and simpler testing in a variety of testing environments that lend themselves to the appearance of do-it-yourself home testing or doctor's office testing by untrained personnel.

None of this technology is foolproof. All of it is subject to the same shortcomings of sloppy laboratory procedures, outdated test reagents, inappropriate storage conditions, inability to follow specific instructions, as well as unfamiliarity with expected results for a positive or negative result.

I could go through some comments on the Cambridge BioScience kit that you have already mentioned vis-a-vis the Wall Street Journal article. We find the same kind of situation with people who are unskilled. These are just indications of the inability of not necessarily unsophisticated but relatively untrained, low volume users to perform an excellent test reproducibly. What can we expect from the general public from use of similar tests in the home environment?

In any event, it is necessary to confirm the test by Western Blot so we do not pick up anything in turnaround time. What assurances do we have that this will even occur? What kind of counseling can we have for persons that self test?

In the current situation, we cannot be certain that the test available for physicians' office use is not being used without Western Blot confirmation, or the patient is not being informed of the screening results.

There are few, if any, convincing arguments for availability of home testing for HIV antibody. In New York State, the State with the highest incidence of AIDS and HIV infection, it is considered a public health imperative to offer free testing that is professionally performed and has an essential element, pretest counseling and posttest counseling.

Testing is only important when accompanied by appropriate counseling for both the uninfected and HIV-infected persons. The only thing that approaches a vaccination against HIV infection for the uninfected person is appropriate information. The only treatment which can be offered for the HIV-infected individual begins with counseling at the same time the person is informed of the HIV antibody result.

I could go on. I just want to indicate that in our laboratory we perform over 600,000 HIV antibody tests per year on specimens for populations with high and low prevalence and maintain an extensive proficiency testing program for all blood banks and related laboratories permitted to perform HIV testing.

With this extensive experience, we view the introduction of this technology to the home environment as being a potential public health disaster. Experience with the difficulty of dealing with HIV antibody testing in a well-controlled laboratory environment that does this large volume of testing leads us to the conclusion that HIV antibody testing, home HIV antibody testing, could well lead to a new public health crisis of additional morbidity and mortality related to the introduction of home test kits.

Thank you.

[Dr. Berns' statement may be found in the appendix.]

Chairman WYDEN. Doctor, thank you. Let me ask you a quick question. We have another vote. I am going to excuse you, and then I am going to come back, and we will finish up with Dr. Johns. You have been just so patient, as well.

I gather, Dr. Berns, that New York has found these nontraditional laboratories kind of moving targets, that they are very difficult to monitor and oversee, and that is why New York felt that it had to move and initiate legislation.

Is that correct?

Dr. BERNs. Yes; we find that there are continual attempts to have situations, such as the previous two witnesses indicated, crop up in New York State.

I personally dealt with many of them that attempt in a very aggressive manner to test in these unconventional environments.

We have, in fact, as a result of this, instituted a group of inspectors, if you will, to go out and look for criminal situations, and we have been successful in Medicaid fraud.

Chairman WYDEN. Your finding is that salesmen often ignore restrictions on who gets test kits?

Dr. BERNs. Yes; as a matter of fact, there are a number of commercial suppliers that have attempted to distribute in New York State, and we have had to act aggressively, call the company nationally, and indicate to them that it was inadvisable to distribute the testing in that environment.

Chairman WYDEN. Do you feel that there is a significant likelihood with home test kits that if they were allowed to be used on a widespread basis then a significant number of unqualified people would be performing these tests?

Dr. BERNs. Undoubtedly. It is a great fear. There is no doubt that suicide will occur. There is no doubt misinformation will be rampant. There is no doubt that many schemes will crop to help, quote unquote, treat these people who have a putative positive test. It is a potential public health nightmare.

Chairman WYDEN. You have been very, very helpful to our subcommittee, and I thank you. I know you are late. I have to go and vote, so, we will excuse you at this time. Dr. Johns, I will try to get back just as fast as I can, and I thank you for your patience. Dr. Berns, thank you.

[Recess.]

BEST AVAILABLE COPY

Chairman WYDEN. The subcommittee will come to order. Doctor, thank you very, very much again for your patience. You have come a long way, and we are very appreciative.

We will make a copy of your prepared remarks part of the record in their entirety, and if you could summarize your principal concerns, that would be very helpful.

TESTIMONY OF PATRICIA A. JOHNS, PH.D., FLORIDA DEPARTMENT OF HEALTH AND REHABILITATIVE SERVICES, OFFICE OF LICENSURE AND CERTIFICATION

Dr. JOHNS. Yes; I will try to be very brief, since it is so late in the day.

I do thank you for the opportunity to testify. I am representing several entities in Florida.

We have had a clinical laboratory law since 1949. It paralleled with the Medicare statute and was revised in 1967 so that it is very much like that legislation.

In recent years, our State has experienced problems with the unconventional screening facilities, some of which are mobile. But the cholesterol screening issue in our State has been the first real challenge to our law in its 40-year history.

The first cholesterol screening company appeared in Florida in early March 1988. Our office received numerous calls of protest from clinical laboratories and equally as many calls from people who wanted to start similar businesses. Approximately 20 cease-operation orders have been sent to such entities in the last year. One of these has resulted in an injunction being served on one of the companies.

The concerns of the Office of Licensure and Certification, for which I work, are about screening operations in general, and I think this is pertinent to both cholesterol screening and HIV screening, or any other kind of screening. These are:

How do these entities obtain instruments specified by the Food and Drug Administration as instruments to be sold to professional persons or organizations only?

How can we be sure that these instruments are calibrated?

Are nonprofessionals aware of the importance of quality control and other testing aspects that can lead to erroneous results?

Are company representatives aware of community resources available to people who should have consultation, and are they providing that information to those that they test?

Are nonprofessionals aware of potential infection hazards to the public and to themselves in handling and disposing of blood saturated materials?

Are they and their organizations easily traced and identified?

What followup is provided when abnormal results are obtained?

Florida expects some measure of regulation in the next legislative session. In fact, as we speak, a bill is being drafted. It is anticipated that the laboratory field will demand that all types of instrument tests be confined to licensed clinical laboratories and that noninstrument tests which are qualitative screening be limited to professional personnel in other disciplines such as nursing, pharmacy, and possibly to dietitians.

I would point out to you that I provided a resource to you, and I commend the entire report to you, the Report of the Study Committee on Cholesterol Screening, published February 1, 1989.

It is a very good report, and I think that you will find some points that have been made already in this hearing may be found there.

I would particularly like to point out to you on page 3 that one of the concerns of this group is that in addition to asking how cholesterol testing can properly be expanded, concern must be given to how this expanded testing can be targeted to reach those groups needing it most, minority groups, for example.

Many of the entrepreneur type of operations are setting up in malls and pharmacies, and they are targeting themselves toward the middle class person who has the \$7 to pay for the test.

Recently, we had a comprehensive AIDS law passed in Florida that came into effect July 1988.

That law requires that there be informed consent including pre- and posttest counseling for the HIV antibody test, that all tests performed are performed in a licensed laboratory, and that there is confirmatory testing prior to reporting positive results.

We have noticed in Florida that there has been advertising for some quick HIV antibody test results, and you had an example in one of the gentleman here today.

However, I think that we are having more trouble with other types of screening at the moment.

Section 381.609 of the AIDS law does require that the test be performed in a clinical laboratory, and this would prohibit any testing in a physician's office, or an unlicensed mobile laboratory, or in the home.

I would also like to point out that Florida has a very comprehensive counseling and testing partner notification program that provides confidential and anonymous HIV antibody testing in its 67 HRS public health units.

We feel that if this is farmed out to mobile units, that this same kind and quality of counseling will not occur.

Because the HIV epidemic is still unfolding, it is vital that epidemiological and demographic information be analyzed.

Mandatory reporting is only required in Florida for a diagnosed AIDS case, and not when you have the instance of the HIV infection.

However, it is important that this kind of demographic and epidemiological information be collected.

In 1988, there were 81,000 such cases identified in our county health units. Access to such important information would be limited if the tests were run in laboratories other than those included in the current system.

I want to thank you for the opportunity to testify, and if you have questions, I will be glad to try to answer them.

[Dr. Johns' statement, with attachments, may be found in the appendix.]

Chairman WYDEN. Doctor, thank you very much. The Florida Health Department has been of enormous help to this subcommittee as well. We very much appreciate your efforts in particular to try to make sure that health delivery meets the high standards

which citizens expect and, frankly, the Florida residents and the many tourists who come to Florida expect, also.

Let me ask some questions regarding AIDS testing that is done in the State and also with respect to the mobile laboratory situation.

It is my understanding that in the early part of 1988, the State found that there was a company that was drawing blood in homes, boats, massage parlors, and in front of 7-Eleven's for purposes of AIDS testing.

Is that correct? If so, what happened to this operation, and would you tell us a little bit about their activities?

Dr. JOHNS. They have ceased. We did find out about that, and we have ceased operations with them. They generally were located in the southern part of our State, and I think they primarily were preying in that area where there is a high-risk group of people. We have given them a cease order which they have complied with.

Chairman WYDEN. Has the State identified other operations where AIDS testing is being conducted, some for example that advertise that they will come to your home to draw blood and send it away to a laboratory?

Dr. JOHNS. Yes; and here again, when we find them we have given them cease orders. We have about three or four such entities included in the 20 cease orders.

Chairman WYDEN. Is it possible that there are more?

Dr. JOHNS. Yes; I suspect there are. They spring up perhaps overnight, and we catch them by seeing their advertisements, or they are reported to us. It is very difficult to find them. They are mobile, and they are hard to monitor.

Chairman WYDEN. Is it your sense that if home testing is permitted on a widespread basis, there are going to be more of these kinds of operators who seem to be exploitive and less interested in good medical care than a fast buck?

Dr. JOHNS. I think probably so.

Chairman WYDEN. What is your assessment of the AIDS quick tests, Doctor, such as the Cambridge BioScience test?

Dr. JOHNS. We would not like to see that used without confirmation. The value, I think, of the quick test is an immediate result. If you are going to tell a patient or a person that you are positive without confirmation, I think that is very unwise. Therefore, the quickness of the procedure is eliminated. If you say well, wait until I send this out, the person is going to know that something is wrong. So, I do not know that is going to be of any great value, because I think confirmation is very important.

Chairman WYDEN. Do you think that kind of test ought to be used in a facility like the one that was here with us today from Florida?

Dr. JOHNS. If they can comply with our regulations, we would not object. But we would like them to meet the requirements for clinical laboratories.

Chairman WYDEN. Do you think that this kind of test encourages the fast buck kind of artists who are concerned that they can get these testings done quickly, just on the basis of screening?

Dr. JOHNS. I think it could. I am not saying that everyone who uses them is doing that, but it certainly could encourage that kind potentially.

Chairman WYDEN. How many anonymous testing sites does the State operate for AIDS testing?

Dr. JOHNS. Under the new law, 67 have been established. They are anonymous, and they are free.

Chairman WYDEN. Is it your view that the State has basically been able to test whoever wanted to be tested?

Dr. JOHNS. I think that it is available; yes.

Chairman WYDEN. What is your sense of why people would go to other facilities?

Dr. JOHNS. Perhaps they are embarrassed to go to a health department. That has been voiced. I know of no other reason. I think that it is essential that they go to someplace where they can get counseling. I shudder to think of counseling over the phone in these kinds of instances, because I think you are dealing with potential suicides and all manner of things.

Chairman WYDEN. It is moving us away from the subject at hand, but I gather from your testimony that your State has experienced other problems with nontraditional screening facilities.

Dr. JOHNS. Yes; we have, particularly in the cholesterol area. When we find them, we have been able to stop them, because we do have a clinical laboratory law. But if they are mobile and moving about, sometimes identifying them initially is difficult.

I would like to say that whether it is HIV screening, or cholesterol, or whatever the hot topic will be tomorrow, I believe that it would behoove the subcommittee to look into screening in general, because I think it is certainly open for entrepreneurs to get into the business, whatever the hot thing might be.

Chairman WYDEN. That is very much our concern with the mobile laboratories in particular.

Is it your sense that the FDA has been responsive to the concerns of the States, your State and others, on these kinds of matters?

Dr. JOHNS. They have written to us when we wrote—Ms. Phillips wrote to them asking for some information about how these instruments could be marketed. The instruments have been marketed in our State to other than professional organizations or professional people or facilities. That has been a problem in our State.

Chairman WYDEN. Do you think more Federal controls ought to be placed on who can get those machines?

Dr. JOHNS. That would be helpful, and enforcement of that.

Chairman WYDEN. And that the FDA should do more in this area to enact controls?

Dr. JOHNS. I would think that would be helpful.

Chairman WYDEN. Well, you have had extraordinary patience. Rarely have we had a hearing go quite this long. I want to thank you very, very much for your patience and for the efforts that you made in working with our subcommittee.

Unless you have anything that you would like to add, we will excuse you at this time.

Dr. JOHNS. Thank you.

Chairman WYDEN. The Subcommittee on Regulation, Business Opportunities, and Energy stands adjourned.

[Whereupon, at 3:07 p.m., the subcommittee was adjourned, subject to the call of the Chair.]

APPENDIX

Third District, Oregon

News From Congressman Ron Wyden

2452 Rayburn House Office Building

Washington, D.C., 20515

(202)225-4811

OPENING STATEMENT
HEARING OF THE SUBCOMMITTEE ON REGULATION, BUSINESS
OPPORTUNITIES & ENERGY
REP. RON WYDEN

TESTING FOR AIDS-HIV IN UNTRADITIONAL LABORATORIES
AND IN THE HOME

March 23, 1989

Today, the Subcommittee on Regulation, Business Opportunities and Energy will examine the potential and the risks of testing for the AIDS-HIV virus in non-traditional laboratory settings.

This is an issue of growing importance because of the increase in requests by manufacturers to market home test devices for use by those who want to know whether they are carrying this deadly virus. Last month, Dr. Frank Young, Commissioner of the U.S. Food & Drug Administration, announced that he would hold a hearing to examine his agency's policy with respect to the licensing of AIDS home tests.

AIDS threatens the lives of millions of Americans. Given this threat, the federal government has a moral obligation to assist medical science in bringing to bear all possible technological power against this dread disease. Any responsible initiative that holds promise in turning back the incidence of AIDS must be implemented by government policy makers.

But the chair is convinced that in the hands of the untrained, the unscrupulous and the insensitive, home AIDS testing can inflict considerable human damage.

-- In the hands of the untrained, there will be more inaccuracies in AIDS testing.

-- In the hands of the unscrupulous, these tests can be used to violate confidentiality, and make a fast-buck by exploiting the fears of our citizens.

-- In the hands of the insensitive, those tested may not receive good counseling and patients may quickly interpret positive results as a virtual death warrant.

There is no doubt that evolving testing technology is driving both non-traditional lab, and home-test approaches to diagnosing AIDS.

A quick, relatively cheap screening test for AIDS, manufactured by Cambridge BioScience, already has been licensed by the FDA for clinical use. More quick test products are likely to follow.

Witnesses today will express concern that it may be difficult to keep this test out of the hands of unqualified persons. Some witnesses will say it has already happened.

We will learn today that the FDA already has told one Cambridge BioScience customer in Texas to abandon plans to use the screen in "improper" home testing. Another storefront lab customer faces action by the state of Florida for alleged violation of that state's AIDS testing laws.

These new diagnostic technologies are part of the drive behind entrepreneurial demands for home testing.

These kits have a place, now, in the health care industry. They can be used by blood banks, by emergency medical technicians, and by doctors in their professional offices. However, government and private industry must guard against their misuse by persons interested primarily in turning a quick profit.

Let me point out that the subcommittee staff has discussed these matters with Cambridge BioScience and their marketing arm, as well as with company representatives in Washington, D.C. The firm and its associates have declined to testify at today's hearing, but let the record show that our report will be kept open for written statements which may be submitted at a later date.

This is the fourth in a series of hearings by the subcommittee on the quality of medical testing. In October 1987, the subcommittee revealed high rates of false positive and false negative results, particularly among low-risk groups. These came even under the best of HIV testing conditions at licensed, professional medical labs.

To quote a New York Times editorial citing this problem: "What should an enlightened society do about a health test that can do as much harm as good?"

The verdict is still out on the reliability of home AIDS testing. But the marketplace demand for a quick, anonymous answer to the AIDS question has not waited for a solution to the problem of inaccurate clinical lab results. The explosion in non-traditional testing activity has encompassed mobile labs, storefront diagnostic centers, and specimen-drawing facilities in health spas and massage parlors.

The American people have a right to expect that their government will take responsible steps to make sure that testing in this critical health care field promotes good medicine. This subcommittee will work closely with the FDA and with the private sector to assure that that obligation is met.



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

STATEMENT
OF
FRANK E. YOUNG, M.D., PH.D.
COMMISSIONER
FOOD AND DRUG ADMINISTRATION
PUBLIC HEALTH SERVICE
DEPARTMENT OF HEALTH AND HUMAN SERVICES

BEFORE THE

SUBCOMMITTEE ON REGULATION AND BUSINESS OPPORTUNITIES
COMMITTEE ON SMALL BUSINESS
U.S. HOUSE OF REPRESENTATIVES

MARCH 23, 1989

RELEASE ONLY UPON DELIVERY

Mr. Chairman:

I am here today at your invitation to address issues related to home test and blood collection systems for detection of infection with the human immunodeficiency virus (HIV).

The Food and Drug Administration (FDA) has been involved actively in the enormously complex issues related to these diagnostic kits. We want to ensure that all of the questions will be answered about the public health implications of their use. We have maintained consistently that these complex issues must be addressed adequately before any such products are considered for consumer use.

Consequently, we have scheduled an open public meeting on April 6 to give experts from FDA, other Government agencies, research institutes, and the private sector the opportunity to discuss the criteria that would need to be met before the Agency would approve AIDS-related home test kits or blood collection kits. We will use these discussions to determine what further course of action the Agency should take, if any. I would like to invite you and your staff to participate in this important meeting.

I am aware of the Subcommittee's ongoing interest in the area of diagnostic testing products and services. Diagnostic products are generally regulated as medical devices but, as I will discuss later, HIV antibody test kits are regulated as biological products. In the home use setting HIV antibody test kits remain a biological product while home blood collection kits would be regulated as medical devices.

While the focus of the hearing today is on home test and blood collection kits specifically for detection of infection with HIV, I believe it would be useful first to describe our authority and broad regulatory framework for the regulation of in vitro diagnostic (IVD) devices.

IN VITRO DIAGNOSTICS

As you know, the FDA generally regulates in vitro diagnostic test kits as medical devices under the Federal Food, Drug, and Cosmetic Act. IVDs are reagents, instruments, and systems that involve the collection, preparation, and examination of specimens taken from the body. They are used, in general, for three purposes: (1) to help diagnose a specific condition or disease; (2) as a screening test to identify indications of disease in people without symptoms; and (3) as monitoring devices to provide ongoing evaluation or analysis of an existing disease or other condition.

The Medical Device Amendments of 1976 provide two basic marketing pathways for medical devices. One mechanism, known as premarket notification or "510(k)", essentially provides for comparing contemporary versions of devices to those marketed prior to 1976. The second process, premarket approval, requires full safety and effectiveness reviews of innovative technologies.

In reviewing devices under the 510(k) process, the Agency makes a determination whether the new device is substantially equivalent to, i.e., is at least as safe and effective as, a previously marketed device.

The other process, premarket approval, requires the device manufacturer to submit full safety and effectiveness data, including comprehensive testing and clinical data for the product, in a premarket approval application (PMA). After a thorough scientific review by appropriate FDA personnel and advisory committees, the Agency either approves or denies the PMA. An approved PMA is, in essence, a private license granted to the applicant to market a particular medical device.

As I mentioned earlier, diagnostic test kits for the detection of infection with HIV are not regulated through the 510(k) or PMA mechanisms. Instead, they are regulated as biological products subject to the licensing provisions of the Public Health Service Act. For these test kits, a Product License Application (PLA) containing information that demonstrates the safety and effectiveness of the product and an Establishment License Application describing the manufacturing facilities, are required. The decision to regulate screening tests for detection of antibodies to HIV as biologicals was made primarily due to the fact that the critical antigen component of the test is derived from a cell-cultured live virus; in other words, the test's critical component is a derivative of a biological product. In addition, these tests are intended to screen blood donations in order to ensure further the safety of the blood supply.

HOME TEST KITS

Traditionally, IVDs have been designed for professional use within a health care setting. More recently, a small number of IVD products have been marketed for at-home, or lay, use. Most of the home-use IVDs currently on the market were cleared for marketing via the 510(k) process, being essentially home-use versions of products previously designed for professional use. These include urine test strips, glucose test meters and strips for use by diabetics, hemoccult tests for detecting fecal occult blood, and pregnancy and ovulation tests. While some of these products were available over the counter prior to passage of the Medical Device Amendments, the review of home-use IVDs, both newer versions of previously marketed devices and those which are based on professional use products, involves consideration of several factors unique to the home use environment. These factors are considered whether the product is being evaluated under a 510(k) or a PMA.

First, in the home environment, users without the technical training of a laboratory technologist may not interpret or follow directions accurately. Second, specimens submitted using a mail-in process may not be submitted in a timely fashion or be protected from temperature extremes or other environmental factors that may affect the test results. Third, unlike clinical laboratory testing, the person performing the test or reviewing the results provided by a laboratory from a mail-in collection kit, usually does not have medical training

to evaluate results in the context of other pertinent medical information. Lastly, the home user may or may not take necessary followup actions on the basis of the test results. Therefore, in evaluating such products, the Agency must consider not only the technical accuracy of the device, but whether the probable health benefits of home use outweigh the probable risks. On the benefit side, we must assess the benefit of the test to the patient and the public health in terms of screening, diagnosing, or monitoring a disease or condition. In addition, it is important to consider the benefits of having such products available to home users as compared with having the test performed only in a health care facility. On the risk side, we are obliged to evaluate whether a layperson can adequately carry out the test, the impact of false-negative or false-positive test results, and the consequences of delay in seeking professional examination or treatment, in cases of a false or equivocal result.

I would like to place in context for you the meaning and significance of false-negative and false-positive results, as well as predictive values, as they apply to IVD tests.

The performance of these diagnostic tests is expressed by the sensitivity and specificity of the test. When a test is 100 percent sensitive it will always give a positive result for those people who have the disease or condition being checked. When it is less than 100 percent sensitive, some people who have the disease will not test positive. These are false-negative results. Measuring sensitivity alone does not give us any information as to how many people who do

not have the disease will test (falsely) positive. In fact, when used in a low prevalence, low risk population, the vast majority of positive results may be false positives, even in highly sensitive tests.

On the other hand, if a test is 100 percent specific, it will always give a negative result for those who do not have the disease or condition being checked. When the test is less than 100 percent specific, it will yield non-specific results and some people who do not have the disease will test positive. These are false-positive results. Measuring specificity alone tells us nothing about how many people who do have the disease will go undetected.

Predictive values have been used to describe the false-positivity and false-negativity of a test in the population being tested. They are the key consideration in determining the clinical usefulness of a test. Because predictive values are influenced by the prevalence of the disease in the tested population, a population in which the prevalence of the disease is low (e.g., less than one percent) may result in a correspondingly high false-positive rate even though the screening device used has an exceptionally high specificity. The predictive value for a negative test result in this same population may be very high, i.e., a low false-negative rate, even though the test's sensitivity may be low. It is important to recognize that a test's sensitivity and specificity usually are constant, whereas predictive values are variable (prevalence dependent) and are relevant only to the population tested.

An ideal test would never give you false-negative or false-positive results. Unfortunately, there is no test that meets these ideal standards. Confirmatory tests are therefore often conducted before test results are discussed with a patient. In considering the effectiveness of an IVD test, the performance of the test in the actual population being screened must also be taken into account.

To regulate home-use IVDs adequately, the Agency sought the input of various industry, consumer, and health professional organizations in the spring of 1985 to help identify the issues that the Agency should consider in evaluating the usefulness, performance, and labeling of such devices. Also, in September of that same year, the FDA held a public hearing and solicited the views of members of a group of our device advisory panels, including the Hematology and Pathology Devices Panel and the Clinical Chemistry and Clinical Toxicology Devices Panel, regarding general issues of the safety and effectiveness of home-use IVDs. The result of these efforts has been the preparation of a draft Points to Consider document regarding labeling and premarket submissions requirements for home-use IVDs. The availability of this document was announced in the Federal Register on November 16, 1988. A copy of each document is submitted for the record. We intend to use this document, both now and with further refinements, as a guide to evaluate the safety and effectiveness of all in vitro diagnostic products intended for home use.

Of course, evaluation of the safety and effectiveness of any medical device, including IVDs, is not limited to just a review of data and information prior to marketing. We have recognized consistently that even the most rigorous premarket approval requirements cannot predict all of the possible adverse effects and potential uses and misuses of a device once it is marketed. Therefore, we have developed an extensive Post Market Surveillance (PMS) system. The various programs that comprise the PMS system are designed to provide the Agency with an early warning of emerging hazards that could affect the public health adversely and to monitor the safety and effectiveness of marketed devices. You may already be familiar with some of the components of this system, such as the mandatory Medical Device Reporting (MDR) regulations which require device manufacturers to inform FDA when their devices are associated with adverse events.

However, it is important to point out that in the case of home use IVDs, the Agency does not receive many reports of adverse incidents from manufacturers under these MDR regulations, probably because of under-reporting of problems with these devices by consumers to the manufacturers or health care professionals. A notable exception is home-use blood glucose meters used by diabetics to regulate insulin dosages. In that case, problems associated with the device or the use of it can result in adverse health consequences requiring immediate medical intervention. As a result, these problems are being reported

to the manufacturers and to FDA. Since we do not receive large numbers of such reports for most home-use IVDs, we would not anticipate receiving any greater number for home test and blood collection systems for detection of infection with HIV. In addition, the issues of confidentiality and anonymity may complicate such reporting.

Also, FDA's field investigators routinely inspect device manufacturers to assure compliance with Good Manufacturing Practices. The need to coordinate information from all parts of the PMS system has resulted in the development of a unified approach to post-market product management (PMPM). This PMPM system begins with efforts to acquire information about the performance of devices as mentioned above and provides for the systematic organization, review, and action on PMS data to ensure that the public is protected from unsafe, ineffective, and improperly used devices.

HIV ANTIBODY HOME TEST KITS

I would now like to address the specific issue of HIV antibody testing in the home environment. As you know, the medical device industry has shown interest in marketing test kits that would allow individuals to draw their own blood and mail it to a laboratory for HIV antibody testing. Such a blood collection kit would be regulated as a medical device, requiring a PMA.

In addition, some manufacturers would like to develop test kits designed to allow individuals to both collect and test their own blood for the HIV antibody at home. As previously mentioned, this type of test kit, containing a biological product derivative, would be regulated as a biological product and require a PLA.

Most of the consideration for home-use in vitro diagnostics are the same for home-use blood collection kits for AIDS. FDA has consistently expressed a number of concerns about the safety and accuracy of these proposed home blood collection kits and home test kits, since their use relies heavily on nonprofessionals who may not have the experience or the training to know how to properly perform or interpret test results. Our concerns led us to write letters, beginning in March 1988, to those firms that had expressed interest in or submitted applications for these kits. I will submit a sample letter for the record. The purpose of these letters was to advise the firms of our present policy concerning applications for these devices, including our decision to accept for filing only those applications that involve kits labeled and marketed for professional use only. We also indicated that we would hold a public meeting at a future date to address and explore our concerns with these products.

To honor that commitment, we have scheduled a public meeting on April 6. In announcing the meeting, we posed a number of questions and concerns with regard to the collection and mail shipment of blood samples by laypersons. We are also concerned with the return of test results to the person from whom the sample was collected and problems

related to interpretation of the results by nonprofessionals and followup counseling if needed. In the instance of a home test kit, we stated our concerns about whether a layperson can reliably and safely perform the test and interpret the results without the benefit of medical advice and professional counseling. We are submitting a copy of the Federal Register announcement of February 17 for the record.

You have raised many of these very same questions in your letter of invitation to this hearing. I believe it is only fitting, on a subject so important, to provide a public forum to discuss and solicit input on how and whether HIV antibody test kits for home use may contribute to or detract from the public health. Our desire is to encourage and participate in a healthy debate as we review policies concerning HIV antibody test kits and their potential usefulness in the struggle to diagnose and combat the spread of the AIDS virus. Again, I extend an invitation to you and your staff to join us in discussion of these issues at the April 6 public meeting.

This concludes my prepared statement. I will be happy to answer any questions you may have.

Assessing the Safety and Effectiveness of Home-use

In Vitro Diagnostic Devices (IVDs):

Draft Points to Consider Regarding Labeling and Premarket Submissions

Center for Devices and Radiological Health

October 1988

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Assessing the Safety and Effectiveness of Home-Use
In Vitro Diagnostic Devices (IVDs):

Draft Points to Consider Regarding Labeling and Premarket Submissions

I. Purpose

The purpose of this document is to assist prospective manufacturers, producers, and marketers (hereinafter called manufacturers) of home-use in vitro diagnostic devices (IVDs) in complying with existing labeling regulations, e.g., 21 CFR 801.5, 809.3(a) and 809.10, and premarket clearance requirements, e.g., Sections 510(k) and 515 of the Federal Food, Drug, and Cosmetic Act (the Act), and regulations including 21 CFR Parts 807 and 814. This document addresses home-use testing kits and home-use mail-in specimen collection kits.

II. Background

In vitro diagnostic devices (IVDs) as defined in 21 CFR 809.3(a) are those reagents, instruments, and systems intended for use in the diagnosis of disease or other conditions, including a determination of the state of health, in order to cure, mitigate, treat, or prevent disease or its sequelae. These products are intended for use in the collection, preparation, and examination of specimens taken from the human body.

Traditionally, IVDs have been used primarily by hospitals, clinical laboratories and physicians' offices. In recent years, however, there has been increasing interest in home-use IVDs, where no physician is involved to interpret the test results.

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Because of this growing interest, FDA's Center for Devices and Radiological Health (CDRH) anticipates receiving an increasing number of premarket product submissions, i.e., premarket notifications or premarket approval applications, for these devices. Consequently, CDRH believes that uniform evaluation criteria for home-use IVDs are needed to better ensure that these devices are regulated in a consistent fashion and that consumers are provided with reliable, useful, and adequately labeled products. To this end, in the spring of 1985, CDRH solicited views from various industry, consumer, and health professional organizations to help identify the issues to be resolved by CDRH in developing evaluation criteria for home-use IVDs. In addition, on September 9, 1985, CDRH convened a public meeting of the chairpersons, the consumer representatives, and the industry representatives of the Immunology Devices Panel, the Microbiology Devices Panel, the Hematology and Pathology Devices Panel, and the Clinical Chemistry and Clinical Toxicology Devices Panel. The purpose of this meeting was to solicit the views of these individuals and other interested persons regarding general issues of the safety and effectiveness of home-use IVDs.

The present document reflects CDRH's views on key points to be considered in establishing the safe and effective use of home-use IVDs. These views are significantly based on the input CDRH has received from the aforementioned outreach activities.

III. Factors CDRH Will Consider in Evaluating the Safety and Effectiveness of Home-use IVDs

A. Performance Considerations

A key factor CDRH must consider in assessing the safety and

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effectiveness of home-use IVDs is test performance. Because the great majority of proposed home-use IVDs are likely to be derived from professional-use IVDs, it is expected that there will be a clear and established relationship between the analyte to be tested using the home-use IVD and a specific medical disorder or condition. Because home-use IVDs function essentially the same as professional-use IVDs, their performance characteristics can be defined in terms of traditional performance parameters such as sensitivity, specificity, accuracy, and reproducibility of test results. Nevertheless, the performance of the device in the hands of skilled users may not reflect the device's performance in the hands of lay users. Consequently, manufacturers of home-use IVDs should focus their attention on the following performance considerations:

1. For a given intended use, the ability of the home-use IVD to detect and/or measure a particular analyte of interest (analytical performance) should be comparable to the performance of IVDs intended for the same purpose that are used by professionals in clinical settings;
2. Home-use IVDs should be designed with a view to ensuring that the device's performance will not be appreciably affected by anticipated variation in user technique; and,
3. Home-use IVDs should include a simple method by which the user can reasonably verify that the product's performance meets its design specifications at the time of use. Ideally, a user quality control test should be provided or "built into" each home-use IVD (see 21 CFR 809.10(a)(6).) Omission of such a test or other

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reasonable means of verifying product performance should be justified based on scientific merit.

B. Risk/Benefit Considerations

Home-use IVDs are different from clinical laboratory devices in four important ways: (1) the person performing the test or reviewing the results returned from a clinical laboratory likely lacks the necessary medical training to evaluate other related medical information, such as, pertinent personal or family medical history, other analyte levels, and the results of a complete physical examination; (2) the person performing the test may lack the technical training of laboratory technologists who traditionally have performed laboratory tests and may not interpret directions carefully; (3) the person performing the test may or may not carry out necessary follow-up actions on the basis of test results; and (4) the person collecting a sample of a body specimen and mailing it to a clinical laboratory generally lacks the technical training of persons who traditionally have collected or supervised the collection of body specimens, and supervised the transport of the specimens to the test laboratory. Thus the person may not ensure that the specimen that arrives at the clinical laboratory is in the same condition as it was when it was collected (e.g. ensuring that the analyte to be measured does not degrade because of passage of a long period of time from specimen collection until analysis, or ensuring that a specimen is not exposed to extremes of hot or cold temperatures or other environmental hazards that may affect the test results).

Hence, in evaluating home-use IVDs, CDRH must consider probable health benefits to be gained in the use of such devices compared to the probable risks associated with their

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use. In this context, consideration of benefit and risk is inherent in the evaluation of safety and effectiveness.

When the use of an in-home IVD can be demonstrated to be substantially equivalent, in terms of safety and effectiveness, to a clinical laboratory device when used by a health professional, and the device meets all labeling and other regulatory and statutory requirements, it will generally satisfy requirements for market clearance. When unique issues of safety and effectiveness arise and substantial equivalence cannot be demonstrated, CDRH will nonetheless evaluate benefit and risk factors in making determinations with respect to the marketability of in-home IVDs. For purpose of assessing these benefit and risk factors CDRH will consider the following questions and encourage applicants to provide relevant information in their submissions.

Benefits

1. What is the clinical benefit of the test to the patient or society (public health) in terms of screening, diagnosing, or monitoring a particular disease, condition, or risk factor?
2. What are the benefits to the patient or society of having the test available for home-use as opposed to having the test performed only by health care professionals?

Risks

1. What is the impact on the user or to society of a false-positive or false-negative test result e.g., in

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terms of user follow-up or adverse medical conditions?

2. What are the risks to the user or society in terms of delay in obtaining a professional examination if a proposed home-use IVD that is intended for use on symptomatic subjects gives a false or equivocal result?

CDRH recognizes that for evaluation purposes, responses to these questions can vary based on the type of product being considered.

C. Labeling Considerations

Acceptability of home-use IVD labeling will depend upon whether such labeling meets the criteria for "adequate directions for use" as provided for in section 502(f)(1) of the Act and defined by 21 CFR 801.5, and the requirements of Subpart C of 21 CFR Part 801. In Addition, home-use IVDs will be deemed to be in compliance with the requirements for adequate directions for use if they meet the requirements of 21 CFR 809.10-Labeling for In Vitro Diagnostic Products..

Inherent in the concept of "adequate directions for use" is the need for the labeling of home-use IVDs to be simple, concise, easy to understand, make liberal use of illustrations and drawings, use bold print or other methods to highlight warnings and precautions, and provide color coding of reagent containers whenever practicable.

Labeling for IVDs intended for home and professional use are covered by 21 CFR 809.10. The following elaborates on the

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application of the regulation to the home-use situation and suggests means of accomplishing compliance:

Section 809.10(a)

1. The intended use statement (section 809.10(a)(2)) should clearly indicate on the outside packaging container the type of procedure that is offered, i.e., screening, monitoring, or diagnostic, and the specific disorder, condition, or risk factor of interest for which the test is intended. In addition, a statement also should be presented indicating who should use the test and the conditions for its use, followed by a contraindication statement(s), if necessary.
2. The quantity, proportion, concentration, or activity of each reactive ingredient included with the test kit need only be presented as specified by section 809.10(a)(3) when information is necessary for proper lay use of the test.

Section 809.10(b)

The order and scope of the information specified by this section should be as follows:

1. The intended use statement should reiterate the information required under section 809.10(a).
2. Section 809.10(b)(3), summary and explanation of the test, may be combined with section 809.10(b)(4), principles of the procedure. This combination of sections should include a discussion of both the medical

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benefits and limitations of the test with respect to its intended use in addition to providing a simple explanation of how the test works. Presentation of chemical reactions or formulas are not necessary but may be referenced in the bibliography (section 809.10(b)(13)).

3. A separate information section relating to interpretation of test results, should be presented and include information specified by section 809.10(b)(10), limitations of the procedure. This section should indicate the significance of the test results in light of the test's intended use and provide specific information as to what appropriate follow-up action should be taken by the user. Additionally, this section should explain the meaning of false-positive and false-negative test results and cite possible sources and implications of false results.
4. A separate information section should be presented which identifies any foods, medications, or other possible interfering substances that would affect test results. Such information should specify what substances should be avoided and for how long prior to testing.
5. Information specified in sections 809.10(b)(5), (6), (7), and (8) may be combined into a single information section, i.e., test procedure. All information specified by these individual sections should be presented in the combined section, if applicable, in addition to the following:
 - a. as previously stated, the quantity, proportion, concentration, or activity of each reactive

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ingredient included in the test kit need not be presented unless this information is necessary for proper use of the test. However, such information should be presented elsewhere in a premarket submission for CDRH review.

- b. discussion of specimen collection, preparation, and analysis steps should be enhanced by the use of pictures and illustrations, preferably in color.
- 6. Information specified by section 809.10(b)(9), test results, should be presented. This section also should include trouble-shooting information where applicable.
- 7. Information specified by sections 809.10(b)(11) and (12) may be combined into a single information section, i.e., test performance characteristics. This section should summarize the data (separately) from both the laboratory evaluation and the consumer field evaluation (see III Premarket Evaluation Considerations) and should include a concise discussion of the study protocols used to evaluate the test's performance. Also, discussion and/or presentation of data relative to the test's accuracy should be presented and include false-positive and false-negative levels. Such information should be presented for both the laboratory and the consumer field evaluations.
- 8. Sections 809.10(b)(13), (14), and (15) should be addressed in the same manner as other IVDs.

In addition, CDRH recommends that manufacturers provide users with a toll-free telephone number or an address to write to should questions occur concerning the use of the device.

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Finally, CDRH is concerned that consumers be aware of significant changes in home-use IVD labeling; particularly labeling accompanying high frequency use devices such as home-use glucose test devices. CDRH advises manufacturers to alert consumers of significant labeling changes by including special inserts with device packaging which highlight key labeling changes. Moreover, CDRH advises manufacturers that labeling changes that significantly impact on a device's safe and effective use may require premarket review and clearance by CDRH before commercial distribution of devices bearing such labeling.

D. Premarket Evaluation Considerations

Given the above considerations CDRH recommends that prospective manufacturers of home-use IVDs conduct the following performance studies and submit results to CDRH for review in an appropriate premarket submission:

- A. A laboratory evaluation of the analytical performance of the device, e.g., analytical sensitivity, analytical specificity, accuracy, and reproducibility, should be done by performing standard laboratory measurements using appropriate reference tests. The purpose of this evaluation is to establish the "true" performance characteristics of the device as determined under controlled laboratory conditions; and,
- B. A consumer field evaluation of the device should be conducted to determine the device's performance when used by lay users, unassisted, following instructions provided in the labeling.

CDRH places considerable importance on the outcome of the consumer field evaluation (item B above) in assessing the safety and effectiveness of home-use IVDs. Consequently, the following additional suggestions are offered with respect to the goals.

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conduct, and analysis of such studies.

1. The primary goal of the consumer field evaluation should be to establish comparable levels of test performance for a particular home-use IVD when comparison-tested by both intended users and trained laboratory personnel. It is suggested that split clinical samples be tested by both lay users and trained laboratory personnel with both groups using the home-use IVD. Such testing will simultaneously validate the technical performance characteristics of the device and the device's labeling based on user experience.

2. In order to assess the ability of lay users to properly perform and interpret test results, CDRH recommends that manufacturers provide simple questionnaires to study participants as part of the consumer field evaluation to determine if lay users can read and understand the labeling. For example, a questionnaire could be used to determine if the user understands the purpose of the test, the conditions for its use, the test's limitations, the meaning of the results and appropriate follow-up.

It is recommended that samples of such questionnaires be included in a premarket submission, as well as a tabulation of all study participants' responses to each question.

3. Lay users selected for study should be representative of target users for which a test is intended. A representative study population may require the selection of individuals of varied background,

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education levels, and age groups. Consequently, subjects should be selected for testing based on carefully developed selection criteria. The basis for establishing the selection criteria should be submitted to CDRH along with the study protocol and test results.

4. The number of subjects selected for testing should be sufficient to substantiate that all targeted lay user populations can perform and interpret the test. It is highly recommended that the number of subjects selected for study be based on a statistically valid sampling of relevant lay users and should take into account appropriate demographic factors. Moreover, test results should be analyzed using appropriate statistical methods to demonstrate correlation between lay users and trained technologists performing the test.
5. Ideally, to avoid potential problems of bias during data collection and evaluation of the consumer field study, a double blind design should be used. However, in studies where such a design is impossible or impractical, a single blind approach and other measures to reduce potential bias may be acceptable. The manufacturer should be careful to select the appropriate type of study to ensure that the study will provide appropriate information.

CDRH believes that both prospective manufacturers of home-use IVDs and CDRH reviewers will be better able to evaluate the safety and effectiveness of these devices when supporting information based on the above considerations is submitted to CDRH in an appropriate premarket submission. Moreover, CDRH believes that as a result of these considerations the general public health will be better served

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by the availability of meaningful and reliable home-use IVDs.

10/5/88

Food and Drug Administration**[Docket No. 87D-0119]****In Vitro Diagnostic Devices (IVD's)
Intended for Home Use; Draft Points
To Consider Regarding Labeling and
Premarket Submissions; Availability****AGENCY:** Food and Drug Administration.**ACTION:** Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft document entitled "Assessing the Safety and Effectiveness of Home-Use In Vitro Diagnostic Devices (IVD's): Draft Points to Consider Regarding Labeling and Premarket Submissions." The draft document was prepared by FDA's Center for Devices and Radiological Health (CDRH) to assist persons manufacturing, importing, or distributing IVD's intended for home use to comply

with FDA's current regulations and thereby ensure that such devices are safe and effective. FDA also is making the draft document available to describe to interested persons the issues involved with marketing IVD's intended for home use. FDA is taking this action under the Federal Food, Drug, and Cosmetic Act.

DATE: Comments received by February 14, 1989, will be considered by FDA in preparing a final points to consider document. The draft document and comments received may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

ADDRESS: Written requests for single copies of the draft points to consider document and any written comments to the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-82, 5600 Fishers Lane, Rockville, MD 20857. (Send two self-addressed adhesive labels to assist the Branch in processing your requests.)

FOR FURTHER INFORMATION CONTACT: Thomas M. Tsakleris, Center for Devices and Radiological Health (HFZ-440), Food and Drug Administration, 6757 Georgia Ave., Silver Spring, MD 20910, 301-427-7234.

SUPPLEMENTARY INFORMATION: IVD's, as defined in FDA's regulations (21 CFR 809.3(a)), are those reagents, instruments, and systems intended for use in the diagnosis of disease or other conditions, including a determination of the state of health, in order to cure, mitigate, treat, or prevent disease or its sequelae. IVD's are intended for use in the collection, preparation, and examination of specimens taken from the human body.

In most cases in the past, a physician supervised the collection of specimens from a patient's body and submitted the specimens to a clinical laboratory with instructions regarding which in vitro tests were to be done. Trained laboratory technicians performed the tests using IVD's. The clinical laboratory reported the test results to the patient's physician who then explained and interpreted the meaning of the test results to the patient.

There has been an increasing interest in recent years in the development of certain IVD's for consumers to purchase and use to perform tests on their own body specimens and interpret the results of their own diagnostic tests.

Accordingly, FDA is making available a document entitled "Assessing the Safety and Effectiveness of Home-Use In Vitro Diagnostic Devices (IVD's): Draft Points to Consider Regarding Labeling and Premarket Submissions." Interested persons may submit to the

Docket Management Branch (address above) written comments on the draft document at any time; however, comments submitted by February 14, 1989, will be considered by FDA in preparing a final points to consider document. The comments submitted will be used to determine whether any revisions of the document are warranted. Two copies of any comments should be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. The draft document and comments received may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

Dated: November 5, 1988.

Frank E. Young,

Commissioner of Food and Drugs.

[FR Doc. 88-29605 Filed 11-25-88; 9:45 am]

BILLING CODE 4160-01-M

Advisory Committees; Meetings

AGENCY: Food and Drug Administration.
ACTION: Notice.

SUMMARY: This notice announces forthcoming meetings of public advisory committees of the Food and Drug Administration (FDA). This notice also summarizes the procedures for the meetings and methods by which interested persons may participate in open public hearings before FDA's advisory committees.

Meetings: The following advisory committee meetings are announced:

Dental Products Panel

Date, time, and place. December 19, 1988, 9 a.m., Conference Rm. D and E, Parklawn Bldg., 5600 Fishers Lane, Rockville, MD.

Type of meeting and contact person. Open public hearing, 9 a.m. to 10 a.m.; open committee discussion, 10 a.m. to 4 p.m.; Gregory Singleton, Center for Devices and Radiological Health (HFD-470), Food and Drug Administration, 8757 Georgia Ave., Silver Spring, MD 20910, 301-427-7555.

General function of the committee. The committee reviews and evaluates available data on the safety and effectiveness of dental products and makes recommendations for their regulation.

Agenda—Open public hearing. Interested persons may present data, information, or views, orally or in writing, on issues pending before the committee. Those desiring to make formal presentations should notify the contact person before December 1, 1988,

and submit a brief statement of the general nature of the evidence or arguments they wish to present, the names and addresses of proposed participants, and an indication of the approximate time required to make their comments.

Open committee discussion. The committee will discuss a guide for the preparation and submission of dental endosseous implant premarket approval applications.

Oncologic Drugs Advisory Committee

Date, time, and place. December 19 and 20, 1988, 8:30 a.m., Conference Rm. D and E, Parklawn Bldg., 5600 Fishers Lane, Rockville, MD.

Type of meeting and contact person. Open committee discussion, December 19, 1988, 8:30 a.m. to 4 p.m.; open public hearing, 4 p.m. to 5 p.m., unless public participation does not last that long; open committee discussion, December 20, 1988, 8:30 a.m. to 5 p.m.; David F. Hersey, Center for Drug Evaluation and Research (HFD-9), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-443-4095.

General function of the committee. The committee reviews and evaluates available data on the safety and effectiveness of marketed and investigational human drugs for use in cancer patients.

Agenda—Open public hearing. Interested persons may present data, information, or views, orally or in writing, on issues pending before the committee. Those desiring to make formal presentations should notify the contact person before December 5, 1988, and submit a brief statement of the general nature of the evidence or arguments they wish to present, the names and addresses of proposed participants, and an indication of the approximate time required to make their comments.

Open committee discussion. On December 19, 1988, the committee will discuss: (1) NDA 19-880 Paraplatin® (carboplatin), Bristol Myers, for treatment of stages III and IV ovarian cancer, and (2) FDA requirements for approval of new drugs for treatment of superficial bladder cancer. On December 20, 1988, the committee will discuss: (1) NDA 19-884 Uromitexan® (mesna), Asta Pharma AG, for use with ifosfamide as a uroprotective agent, and (2) supplemental NDA 17-970/S-018 Nolvadex® (tamoxifen), Stuart Pharmaceutical Co., for treatment of premenopausal advanced breast cancer.

FDA public advisory committee meetings may have as many as four separate portions: (1) An open public hearing, (2) an open committee

discussion, (3) a closed presentation of data, and (4) a closed committee deliberation. Every advisory committee meeting shall have an open public hearing portion. Whether or not it also includes any of the other three portions will depend upon the specific meeting involved. There are no closed portions for the meetings announced in this notice. The dates and times reserved for the open portions of each committee meeting are listed above.

The open public hearing portion of each meeting shall be at least 1 hour long unless public participation does not last that long. It is emphasized, however, that the 1 hour time limit for an open public hearing represents a minimum rather than a maximum time for public participation, and an open public hearing may last for whatever longer period the committee chairperson determines will facilitate the committee's work.

Public hearings are subject to FDA's guideline (Subpart C of 21 CFR Part 10) concerning the policy and procedures for electronic media coverage of FDA's public administrative proceedings, including hearings before public advisory committees under 21 CFR Part 14. Under 21 CFR 10.205, representatives of the electronic media may be permitted, subject to certain limitations, to videotape, film, or otherwise record FDA's public administrative proceedings, including presentations by participants.

Meetings of advisory committees shall be conducted, insofar as is practical, in accordance with the agenda published in this Federal Register notice. Changes in the agenda will be announced at the beginning of the open portion of a meeting.

Any interested person who wishes to be assured of the right to make an oral presentation at the open public hearing portion of a meeting shall inform the contact person listed above, either orally or in writing, prior to the meeting. Any person attending the hearing who does not in advance of the meeting request an opportunity to speak will be allowed to make an oral presentation at the hearing's conclusion, if time permits, at the chairperson's discretion.

Persons interested in specific agenda items to be discussed in open session may ascertain from the contact person the approximate time of discussion.

Details on the agenda, questions addressed by the committee, and a current list of committee members are available from the contact person before and after the meeting. Transcripts of open portions of the meeting will be available from the Freedom of



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Bethesda MD 20205

March 29, 1988

Elliott J. Millenson, Chairman PMA Number: BP880001
 University Hospital Corporation (UHL) Product Name: AIDS Check
 4001 North Ninth Street, Suite 1511
 Arlington, VA 22203

Dear Mr. Millenson:

The Center for Biologics Evaluation and Research (CBER) of the Food and Drug Administration (FDA) has completed an initial review of your premarket approval application (PMA). This review revealed that the application contains major deficiencies and cannot be filed at this time. This means that your PMA will not undergo further review until deficiencies are corrected.

As you may be aware, the FDA requested the advice and counsel of various advisory groups and interested parties to assist us in establishing appropriate regulatory controls for the marketing and sale of blood collection kits labeled for AIDS testing. Based on our evaluation of comments and guidance received from advisory groups with knowledge of AIDS related testing issues, we have concluded that, for the present time, only those PMAs that meet the following criteria will be acceptable for filing:

1. Kits must be labeled and marketed for professional use only within a comprehensive health care environment (e.g., hospitals, medical clinics, doctor's offices, STD clinics, alternative test sites, and mental health clinics);
2. Kits must provide for the collection of a venipuncture or other appropriately validated sample by one who is recognized by a state or local authority to perform such procedures;
3. The testing sequence for all samples collected with the kits must include use of a licensed screening test for antibody to HIV and, for those samples testing positive by the screening test, the use of an additional, more specific test (i.e., Western Blot or comparable test). It is recommended that a licensed more specific test be utilized; however, the Agency may accept a properly validated unlicensed test until licensed tests are more widely available;
4. The instructions for sample collection, storage, shipping, and testing must conform with, or be validated as equivalent to, the package insert instructions for the specific licensed HIV antibody test kit used to test samples; and
5. All results of testing must be reported directly to a professional health care provider for reporting and interpretation of the result to the requestor of the test, as well as for counseling of the individual.

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Since your submission requests approval of a blood collection system for AIDS testing to be used by lay persons, it cannot be filed at this time. Additional deficiencies, unrelated to your product's intended use outside of a comprehensive health care environment, include:

- a. Neither the Genetic Systems LAV EIA test kit nor the Biotech/DuPont HIV Western Blot kit contain instructions for using filter paper eluates in testing. Each would need to be validated for use with eluates. Validation requires that the ELISA screening method be performed on a minimum of 3000 low risk outpatients, 100 high risk outpatients, and 50 AIDS patients. Studies should include known AIDS and ARC samples from distinct world-wide locations. All samples found to be reactive and borderline reactive (20% below cut-off) with the ELISA, and a significant number of negative samples, should be tested with the Western Blot. A statistically valid number of samples should be paired to demonstrate comparability between samples collected and shipped by your method and fresh samples collected and tested in accordance with the HIV test kits' package insert instructions. Included in the paired studies, dilution series should be constructed from blood samples from five AIDS and five asymptomatic positive patients to show equivalence by titration endpoints of the sample collection techniques in both the ELISA and Western Blot tests. Stability studies with the blood spot should demonstrate equivalence between eluates from fresh spots and those that have been stored and shipped;
- b. Your submission lists two laboratories, Johns Hopkins School of Public Health and SmithKline Bio-Science Laboratories, for sample receipt and testing. However, study data were submitted from Johns Hopkins only. Each laboratory must demonstrate performance of tests by the methods outlined in your PMA; and
- c. Clinical data must be obtained under conditions representing the product's actual use. For example, our review indicates that study filter paper samples were stored with a desiccant at 4°C prior to shipping. There are no such provisions in the instructions for the use of the collection system.

All collection systems for AIDS testing that meet the criteria in points 1-5 above and the requirements of 21 CFR 809.10(c) [referenced in 812.2(c)(3)] will be considered exempt from the requirement for significant risk devices of filing an application for an investigational device exemption (IDE) prior to undertaking a clinical study. Although under these circumstances an IDE application need not be filed, manufacturers should, however, follow the investigational plan outlined in 21 CFR 812.25, including the provisions for IRB approval, informed consent, and monitoring. We strongly recommend that manufacturers discuss investigational plans and clinical trial protocols with the agency prior to the initiation of investigations.

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Although the criteria outlined in items 1-5 above represent our current approach to the regulation of these devices, we plan to seek further public comment on such issues as lay person sample collection and shipping, and counseling outside of medical settings. We will keep you apprised of matters relating to blood collection kits intended for AIDS testing, including any FDA publication of requests for written public comment or announcements of public hearings.

In accordance with the provisions of 21 CFR 814.42(d), resubmission of the PMA to conform with the above listed provisions or a request for an informal conference with the Director of the Center for Biologics Evaluation and Research to review the decision not to file the PMA shall be identified as a PMA amendment and any correspondence shall include the above PMA reference number. The PMA amendment should be addressed to:

Paul D. Parkman, M.D., Director
Center for Biologics Evaluation and Research, HFB-825
Food and Drug Administration
8800 Rockville Pike
Bethesda, MD 20892

If you have questions concerning this letter, please contact Ms. Mary Gustafson of the Division of Product Certification at (301) 443-5433.

Sincerely yours,



Paul D. Parkman, M.D.
Director
Center for Biologics Evaluation and Research

Board of Tea Experts

Date, time, and place. March 13 and 14, 1989, 10 a.m., Rm. 700, 850 Third Ave., Brooklyn, NY.

Type of meeting and contact person. Open public hearing, March 13, 1989, 10 a.m. to 11 a.m.; open committee discussion, 11 a.m. to 4:30 p.m.; open committee discussion, March 14, 1989, 10 a.m. to 4:30 p.m.; Robert H. Dick, New York Regional Laboratory, Food and Drug Administration, 850 Third Ave., Brooklyn, NY 11232, 212-985-5739.

General function of the committee. The committee advises on establishment of uniform standards of purity, quality, and fitness for consumption of all teas imported into the United States under 21 U.S.C. 42.

Agenda—Open public hearing. Interested persons may present data, information, or views, orally or in writing, on issues pending before the committee.

Open committee discussion. The committee will discuss and select tea standards.

Science Advisory Board to the National Center for Toxicological Research

Date, time, and place. March 23, 1989, 9 a.m., Bldg. 13, Conference Rm., National Center for Toxicological Research (NCTR), Jefferson, AR.

Type of meeting and contact person. Open board discussion, March 23, 1989, 9 a.m. to 10:45 a.m.; open public hearing, 11 a.m. to 12 m.; open board discussion, 1 p.m. to 6 p.m.; Ronald F. Coene, NCTR (HFT-2), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-443-3155.

General function of the board. The board advises the Director, NCTR in establishing and implementing a research program that will assist the Commissioner of Food and Drugs in fulfilling his regulatory responsibilities. The board provides extra-agency review in ensuring that research programs at NCTR are scientifically sound and pertinent to its stated goals and objectives.

Agenda—Open public hearing. Interested persons may present data, information, or views, orally or in writing, on issues pending before the committee. Those desiring to make a formal presentation should notify the contact person before March 6, 1989, and submit a brief statement of the general nature of the evidence or arguments they wish to present, the names and addresses of proposed participants, and an indication of the approximate time required to make their comments.

Agenda—Open board discussion. The board will review the research programs of caloric restriction and human risk assessment. A final agenda will be available on March 20, 1989, by notifying the contact person.

FDA public advisory committee meetings may have as many as four separable portions: (1) An open public hearing, (2) an open committee discussion, (3) a closed presentation of data, and (4) a closed committee deliberation. Every advisory committee meeting shall have an open public hearing portion. Whether or not it also includes any of the other three portions will depend upon the scientific meeting involved. There are no closed portions for the meetings announced in this notice. The dates and times reserved for the open portions of each committee meeting are listed above.

The open public hearing portion of each meeting shall be at least 1 hour long unless public participation does not last that long. It is emphasized, however, that the 1 hour time limit for an open public hearing represents a minimum rather than a maximum time for public participation, and an open public hearing may last for whatever longer period the committee chairperson determines will facilitate the committee's work.

Public hearings are subject to FDA's guideline (Subpart C of 21 CFR Part 10) concerning the policy and procedures for electronic media coverage of FDA's public administrative proceedings, including hearings before public advisory committees under 21 CFR Part 14. Under 21 CFR 10.205, representatives of the electronic media may be permitted, subject to certain limitations, to videotape, film, or otherwise record FDA's public administrative proceedings, including presentations by participants.

Meetings of advisory committees shall be conducted, insofar as is practical, in accordance with the agenda published in this Federal Register notice. Changes in the agenda will be announced at the beginning of the open portion of a meeting.

Any interested person who wishes to be assured of the right to make an oral presentation at the open public hearing portion of a meeting shall inform the contact person listed above, either orally or in writing, prior to the meeting. Any person attending the hearing who does not in advance of the meeting request an opportunity to speak will be allowed to make an oral presentation at the hearing's conclusion, if time permits, at the chairperson's discretion.

Persons interested in specific agenda items to be discussed in open session

may ascertain from the contact person the approximate time of discussion.

Details on the agenda, questions to be addressed by the committee, and a current list of committee members are available from the contact person before and after the meeting. Transcripts of the open portion of the meeting will be available from the Freedom of Information Office (HFI-35), Food and Drug Administration, Rm. 12A-16, 5600 Fishers Lane, Rockville, MD 20857, approximately 15 working days after the meeting, at a cost of 10 cents per page. The transcript may be viewed at the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-42, 5600 Fishers Lane, Rockville, MD 20857, approximately 15 working days after the meeting, between the hours of 9 a.m. and 4 p.m., Monday through Friday. Summary minutes of the open portion of the meeting will be available from the Freedom of Information Office (address above) beginning approximately 90 days after the meeting.

This notice is issued under section 10(a)(1) and (2) of the Federal Advisory Committee Act (Pub. L. 92-463, 88 Stat. 770-776 (5 U.S.C. App. I)), and FDA's regulations (21 CFR Part 14) on advisory committees.

The Commissioner approves the scheduling of meetings, at locations outside of the Washington, DC, area on the basis of the criteria of 21 CFR 14.22 of FDA's regulations relating to public advisory committees.

Dated: February 13, 1989.

John M. Taylor,

Associate Commissioner for Regulatory Affairs.

[FR Doc. 89-3732 Filed 2-10-89; 8:45 am]

BILLING CODE 4165-21-M

[Docket No. 88H-0319]

Blood Collection Kits Labeled for Human Immunodeficiency Virus Type 1 (HIV-1) Antibody Testing; Home Test Kits Designed to Detect HIV-1 Antibody; Open Meeting

AGENCY: Food and Drug Administration.
ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing an open public meeting to discuss blood collection kits and home test kits that are designed to detect antibody to human immunodeficiency virus type 1 (HIV-1). HIV-1 has been identified as the etiologic agent responsible for acquired immunodeficiency syndrome (AIDS). FDA is also inviting written comments on the kits and their use. The

proceedings of the meeting and the written comments will be considered in the development of final policy and regulatory decisions for the matters addressed in this notice.

DATE: The meeting will be held on April 8, 1989, at 8:30 a.m. Requests to make a presentation should be received no later than March 30, 1989. Written comments should be submitted by May 5, 1989.

ADDRESS: The meeting will be held at the National Institutes of Health, Clinical Center, Bldg. 36, Jack Mason Auditorium, 9000 Rockville Pike, Bethesda, MD 20892. Written comments or requests for a copy of the agenda may be submitted to the Dockets Management Branch (HFA-306), Food and Drug Administration, Rm. 4-02, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT:

Regarding the meeting: Debbie Henderson, Center for Biologics Evaluation and Research (HFB-6), Food and Drug Administration, 8600 Rockville Pike, Bethesda, MD 20892, 301-495-0561.

Regarding this notice: Mary Gustafson, Center for Biologics Evaluation and Research (HFB-249), Food and Drug Administration, 8600 Rockville Pike, Bethesda, MD 20892, 301-443-6433.

SUPPLEMENTARY INFORMATION

I. Background

As a result of the recognition of AIDS and the identification of the etiologic agent, HIV-1 (formerly known as human T-lymphotropic virus type III and lymphadenopathy associated virus), there has been extensive interest in the development of *in vitro* diagnostic tests for detecting evidence of infection with the virus.

Tests utilizing enzyme linked immunoassay (ELISA) and Western blot technologies for detecting antibody to HIV-1 have been approved by FDA. Nine manufacturers currently hold licenses issued under section 362 of the Public Health Service Act (the PHS act) (42 U.S.C. 262) for the test systems to be used in test systems to detect antibody to HIV-1 in human serum and plasma samples. The test is used as an aid in the diagnosis of HIV-1 infection and for screening blood. In the Federal Register of January 5, 1988 (53 FR 113), FDA published a final rule requiring that each unit of human blood and blood components intended for transfusion or for use in preparing a product be tested and found negative by an approved HIV-1 antibody test.

In 1986 and 1987, FDA received several submissions under section 510(k) of the Federal Food, Drug, and

Cosmetic Act (the act) (21 U.S.C. 360(k)), notifying the agency of manufacturers' intent to market blood collection kits labeled for HIV-1 antibody testing. Such blood collection kits for nonprofessional use have sometimes been referred to as "AIDS home test kits." The proposed blood collection kits provide instructions and equipment for sample collection, packaging for shipment of the sample to a laboratory for HIV-1 antibody testing and a confidential mechanism for receiving the results of testing.

In receiving the manufacturers' submissions, FDA agreed with the manufacturers that these blood collection kits are medical devices subject to the act. However, FDA determined that blood collection kits labeled for HIV-1 antibody testing are not substantially equivalent to devices marketed prior to May 28, 1976, or to devices classified as class I or II since that date, and therefore are classified by statute in class III and are subject to premarket approval under section 515 of the act (21 U.S.C. 360e). FDA has since received applications for premarket approval and numerous inquiries concerning the marketing of these blood collection kits.

In March 1988, FDA began to notify applicants for premarket approval of home blood collection kits that the agency was limiting the marketing of blood collection kits at this time to those intended for professional use only. FDA's response to the applications and inquiries was developed through consultation with the Public Health Service and private sector advisory groups. Under FDA's policy on these kits, applications for premarket approval are accepted only when they meet the following criteria:

1. Kits are labeled and marketed for professional use only within a health care environment (e.g., hospitals, medical clinics, doctor's offices, sexually transmitted disease clinics, HIV-1 counseling and testing centers, and mental health clinics).
2. Kits provide for the collection of a venipuncture or other appropriately validated sample by one who is recognized by a State or local authority to perform such procedures;
3. The testing sequence for all samples collected with the kits includes use of a licensed screening test for HIV-1 antibody and, for those samples testing positive by the screening test, the use of an additional more specific test (i.e., Western blot or comparable test). It is recommended that a licensed test which is more specific for HIV-1 antibody be utilized. However, the agency may accept a properly validated unlicensed

test until licensed tests are more widely available;

4. The instructions for sample collection, storage, shipping, and testing conform with, or are validated as the equivalent to, the package insert instructions for the specific licensed HIV-1 antibody test kit used to test samples; and

5. All results of testing are reported directly to a professional health care provider for reporting and interpretation of the results to the person requesting the test, as well as for counseling of the individual.

As with any new product, FDA expects that some developmental phase will be needed. If a blood collection kit labeled for HIV-1 antibody testing is developed according to the criteria in 1 through 5 above and to the requirements of 21 CFR 806.34(c), an investigational device exemption (IDE) pursuant to 21 CFR Part 812 will not be required during the developmental stages of the kit. (See also 21 CFR 812.2(c)(3).)

If a blood collection kit labeled for HIV-1 antibody testing is developed under an investigation act incorporating the criteria in 1 through 5 above, FDA views the investigation as requiring an IDE.

A kit for testing at home to detect HIV-1 antibody would include a biological product as defined under section 353 of the PHS act. A manufacturer or sponsor investigating or developing such a kit would be required to have an approved investigational new drug application (IND) and the kit would be subject to licensure under the PHS act.

II. Public Meeting Topics

The public meeting will provide a forum to discuss FDA's policy described above, the following topics, and other topics that may be suggested later:

A. Topic 1: Blood Collection Kits

1. Collection and shipping of blood samples by laypersons. Improper sample collection, preparation, and shipment could adversely affect the accuracy of HIV-1 antibody test results. In addition, it is possible, although most unlikely, that improper sample collection and transport might result in transmission of infection or injury. Therefore, comments are solicited on the ability of laypersons to safely and adequately collect and package these samples for shipment.

2. Return of test results directly to the person from whom the sample was collected. Some manufacturers have proposed systems in which the HIV-1 antibody test results would be returned

directly to the person from whom the sample was collected. The results of in vitro diagnostic tests often require interpretation (e.g., under what circumstances false-negative or false-positive results might occur) and must be integrated into an overall assessment of a person's medical status. Before returning the results of testing for evidence of infection with HIV-1 to any person other than a health professional, adequate instructions for interpretation of the test results would have to be developed. Comments are solicited on whether such information could be adequately provided.

3. *Counseling outside of a medical health care environment.* This topic is related to the issue of proper interpretation of and followup on test results. There is agreement among medical experts that adequate counseling regarding the test results should be part of HIV-1 testing. Comments are solicited regarding the ability to provide effective pre- and post-test counseling in a setting outside the health care environment.

4. *Availability of blood collection systems.* The availability of blood collection systems as over-the-counter (OTC) devices could increase the number of samples tested by making systems more readily available. Comments are solicited on whether blood collection systems should be available as OTC devices.

B. Topic 2: Kits for Collection and Home Testing of Blood for Evidence of HIV-1 Infection

Some have discussed the possibility of developing test kits with which laypersons could not only obtain their own specimen at home, but also perform testing for evidence of HIV-1 infection. FDA invites comments on issues related to these types of kits. Such issues would include whether the kits should be made available OTC, whether laypersons can reliably and safely perform the test, whether laypersons can adequately interpret the test results, and whether that interpretation in the absence of a medical professional is appropriate.

The agenda of the public meeting will provide an opportunity for all interested persons to make their views known to FDA and to allow thorough discussion of the issues. However, FDA requests that interested persons intending to make formal presentations notify the information contact person (identified above) no later than March 30, 1989, so that the available time may be allotted among the persons making the requests.

Interested persons may submit written comments or requests for a copy of the agenda for the meeting to the Dockets

Management Branch (address above). Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments on matters discussed in this notice and presented at the meeting or written comments received by May 3, 1989, will be considered in developing a final policy. Comments and requests for an agenda are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

Dated: February 6, 1989.

Frank E. Young,
Commissioner of Food and Drugs.
[FR Doc. 89-3734 Filed 2-10-89; 8:45 am]
BILLING CODE 4160-01-M

[Docket No. 84H-0241]

Availability of 1988 Revision of the
National Shellfish Sanitation Program
Manual of Operations, Parts I and II

AGENCY: Food and Drug Administration.

National
Organizations
Responding to
AIDS

TESTIMONY OF

GAIL HARRIS

Project Director, National Resource Center on Women and AIDS

Center for Women Policy Studies
Washington, D.C.

On Behalf of the

NATIONAL ORGANIZATIONS RESPONDING TO AIDS (NORA), PREVENTION TASK FORCE

before the

UNITED STATES HOUSE OF REPRESENTATIVES

SMALL BUSINESS SUBCOMMITTEE ON REGULATION, BUSINESS OPPORTUNITIES AND ENERGY

on the subject of

HOME TEST KITS FOR AIDS ANTIBODIES

MARCH 22, 1990

The Honorable Ron Wyden, Chair
3300 A Rayburn House Office Building

a coalition convened by

AIDS ACTION COUNCIL

2033 M Street, N.W. • Suite 801 • Washington, D.C. 20036
(202) 293-2886 • FAX (202) 296-1292

Mr. Chairman and members of the Committee, my name is Gail Harris, I am the Project Director for the National Resource Center on Women and AIDS through the Center for Women Policy Studies. I am here today on behalf of the National Organizations Responding to AIDS (NORA), a coalition of over 120 national health, governmental, social service, education and civil rights agencies. The NORA Prevention Task Force, known as the Coalition for AIDS Prevention and Education, welcomes this opportunity to comment on the issues relating the licensing of home test kits for the AIDS antibody. Since the advent of the AIDS antibody test in the spring of 1983, no issue has more clearly captured the nature of the public debate around this epidemic than the appropriate use of the test. Now, the Congress is reviewing the public and scientific record in light of the Food & Drug Administration's (FDA) consideration of licensing of home test kits for the human immunodeficiency virus (HIV). NORA applauds the Committee's interest in addressing such a critical issue of AIDS policy and notes its serious reservations about the licensing of a product which may have an adverse impact on the public health response to the epidemic.

While there are a myriad of concerns attendant to the licensing of the home test kit, NORA is particularly concerned about its impact on the public health issues of behavior change, mental health and access to primary health services. We recognize that significant biomedical questions, such as the reliability of the sampling process and the validity of the testing

procedures must be resolved, before any sound public policy decisions can be made.

Behavior Change

In 1986, 24 national professional organizations joined, under the auspices of the Coalition for AIDS Prevention and Education (CAPE) in issuing the first consensus statement on the appropriate use of the HIV antibody test and the inseparable need for quality counseling. Co-signers of this statement included the American Psychological Association, the American Hospital Association, the American Nurses' Association, the National Association of Social Workers, the National Association of Counties and the American Federation of State, County and Municipal Employees. A copy of this statement is enclosed for the record.

The CAPE statement argues that stopping the transmission to HIV is an urgent public health goal. Such prevention requires behavioral change which can only be accomplished through education and counseling. The statement points to research which indicates that behavior change is most effective when the decision to change behaviors is voluntary. Tools such as the HIV antibody test may be an appropriate adjunct to a voluntary program of behavior change. Testing in and of itself, however, is of little use—it is only as good as the education and counseling that accompany the test. Obviously, testing by itself will not achieve the public health goal of behavior change—people need to be told how and encouraged to change their

behavior. Indeed, we have some data which suggests that in the absence of counseling, people will continue to engage in high risk activities.

In some cases, HIV-antibody testing will be an appropriate adjunct to a counseling strategy for facilitating behavior change or as a source of information necessary for effective decision making. If testing is used, the individual must be given the opportunity to work through the psychological issues raised by the testing. However, testing in and of itself is not a goal—it is only a means to preventing further transmission. The marketing of a home test kit appears to reflect a response completely contrary to this goal, one that emphasizes testing, possibly at the expense of counseling.

According to the CAPE coalition document, a good counseling and testing program involves: 1) educating people about the means of transmission and methods of reducing risky behavior; 2) pre-test counseling; and 3) extensive post-test counseling. A more detailed outline of the steps in such a process are outlined in the CAPE position paper. Counseling involves individualized assessment of risk behaviors, facilitation of effective decision making concerning appropriate behavior change, and resolution of psychological and social problems raised by this process. Other witnesses today will more fully explore these behavior change issues. Both the pre- and post-test counseling pieces are important because they help provide a context in which the client can interpret his or her results. Without the pre-test piece, the post-test counseling may completely miss its mark as the

uninformed infected client receives devastating information. As outlined in public documents, it is unclear as to whether home test kits would meet this test.

According to CAPS, during the pre-test phase, the counselor should assess the client's degree of risk, and recommend specific behavior changes. In addition, the counselor should obtain the client's informed consent to submit to testing, an agreement which shows that the client has understood the negative social, legal and psychological ramifications of the test as well as its positive effects. Many persons who might otherwise be interested in testing may decide against such a course if they recognize the potential for HIV-related discrimination. None of these procedures would be adequately addressed in the context of an home testing protocol. Many individuals who might be encouraged to test through provocative or enticing advertisements might only find out about the dangerous legal and social problems following the testing process.

Mental Health Issues and the HIV Test

One of the most critical issues around home test kits is the ability of such a program to adequately meet the psychosocial needs of the tested population. During the post-test phase, the individual should be assisted in working through any adverse psychological reactions and reducing resistance to behavior change. For some time now we have been aware of the serious adverse effects of testing. In order to address these adverse

effects, the counseling component must not only focus on behavior change but also the mental health concerns of the client.

Following testing CAFE agrees that clients should be referred to other therapeutic programs such as substance abuse treatment, on-going mental health counseling or peer support groups as necessary. Realistically, such a process cannot be achieved through anything less than in-person contact. Whether the home test kit protocol can meet this pressing need remains unclear. Indeed, as the serious mental health implications of the test have become more apparent, there is reason to believe that the short, hour-long post test counseling session which reflects the standard of care in most health care institutions, may not be enough to stem the adverse mental health issues which develop as a function of an HIV test.

Moreover, we oftentimes forget how important post-test counseling is for the HIV-negative individual. These are the people who are free of the virus and we must ensure that they remain uninfected. In a New York study, 30 per cent of a group of HIV negative individuals who had not received counseling thought that they had successfully fought off the virus and were not at risk from future exposure. Following counseling, all of these individuals have become aware of their future risk of infection. But equally important, post-test counseling and referrals to on-going services may help to alleviate some of the more serious psychological consequences of testing.

As I have noted, data has been accumulated over the last several years indicating that adverse social and psychological consequences are associated with knowledge of one's seropositive status. The consequences include severe depression, breakups of relationships, social isolation, and disabling levels of anxiety. As more testing has been done throughout the country, however, anecdotal reports have begun to surface about HIV-testing-related suicides. From the Health Crisis Network in Florida, we have a report of a young man who upon learning of a positive test result killed himself. Tragically, an autopsy indicated that the positive test result was incorrect—a function of the margin of error in the HIV test. Nevertheless, if this young man had received adequate counseling, his life might have been spared.

From New York, we have heard the all-too-often report of the young college-aged man who had experimented with homosexuality but was far from deciding about his sexuality. He was tested by a family physician who provided no counseling. When the young man presented himself to the therapist, he was convinced of his imminent death, had put his entire life on hold including plans for law school and was seriously contemplating suicide. Fortunately, for the second individual, counseling became available and the client has successfully adjusted his life to the fact that he is HIV-positive. These stories which are typical of the dramas occurring across the country as a function of this disease, call out for the need to pay close attention to the mental health needs of persons tested for the

AIDS virus. Without adequate counseling, one can only speculate as to the frequency of such incidents following home testing.

A Review of Telephone Counseling Literature

The manufacturers of the home test kits have placed a great deal of emphasis on the value of the telephone counseling they will provide to all test subjects. In a brief review of the literature, it appears that the data about the efficacy of telephone counseling is spotty at best. Numerous studies exist assessing the non-HIV related telephone counseling programs through self reported satisfaction scales, however, very few rigorous studies involving the use of control groups or random assignment have been completed. This strongly argues that the efficacy of such programs remain in great question. No data exist on the impact of HIV testing related telephone counseling and such a program could only be marketed on a large scale basis a great risk to the client population without further study.

In the research literature, no identical paradigm exists for the type of service contemplated with the HIV testing/phone counseling program. However, some observations may be made. One study reported in Hospital and Community Psychiatry (July 1986, v. 37(7)), reported that there is currently no evidence that telephone counseling produces behavior change in callers or reduces suicide rates although such services may have a therapeutic value for monitoring or supporting clients with on-going problems. Another study addressed the issue of behavior change and telephone counseling. In looking

at telephone aftercare for alcoholics discharged from inpatient facilities, the study showed that although the patients reported a satisfaction with the program, there was no indications of higher on-going rates of recovery among those receiving telephone counseling and only one subject out of 123 indicated that the service helped maintain sobriety. All of which suggests concerns about the value of telephone counseling to modify behaviors, particularly those that are deeply ingrained and reinforcing such as substance abuse or sexual behavior.

In the area of mental health, The Canadian Journal of Psychiatry ran an article in 1981 (October, v. 26(8)) which indicated that in a comparison of two different telephone suicide prevention programs, there was no indication that the telephone services lowered the suicide rate. Moreover, several studies have suggested that to be effective, such service must operate within in the context of the network of other existing community service programs. Whether the AIDS home test kit program could provide referral services to persons across the country is obviously an important policy question.

Many of these issues were fully articulated in a paper written by Thomas Nagy, chair of an ethics task force for the American Psychological Association's (APA) in 1987. The article provided some guidance for psychologists contemplating using the telephone as means of delivering mental health services. In it, Nagy stated that, "as a rule, ongoing counseling or psychotherapy via telephone or computer as a primary goal, in

the absence of initial or planned ultimate face-to-face contact may not constitute sound ethical practice." The reason for this rather complete disavowal, is the fact that the physical nature of the telephone "may block information essential to a differential diagnosis, resulting in a possible diminished quality of care for certain patients." In conclusion, Nagy argues that psychologists should "refrain from advertising or offering psychotherapy over the telephone in the absence of a client's compelling psychological or physiological evidence that would preclude an office visit."

AIDS Testing and Linkage with Health Care Services

In its recommendations, the Coalition for AIDS Prevention and Education (CAPE) argues that routine education and counseling should be made available by the federal government to all people who enter family planning, prenatal, sexually transmitted diseases, and drug abuse clinics. Such counseling should also be routinely available at alternative test sites. One of the central features of this connection between testing and other collateral health services, is the importance of linking the treatment of HIV infection with other aspects of primary health care.

With the advent of AZT, some researchers and doctors believe it is now possible to use medical interventions to delay the possible progression of HIV-related symptoms. Unfortunately, the potential for improving the medical outlook of the disease is not equally available to all. Many

individuals do not have access to the information, medical interventions, and mental health services which make early treatment possible. Testing positive to the HIV antibody will require other follow up medical tests that are necessary for determining proper medical intervention.

Without proper interaction with the health care delivery system during the counseling process, there is no assurance that a patient with an HIV infection would receive the appropriate medical or psychological follow-up. With a home test kit, the patient or client may be entirely lost to the health care delivery system. This problem may be particularly acute within minority and poverty communities, where the lack of access to proper health care services continues to be a major cause of greater rates of AIDS-related morbidity and mortality.

This lack of access to health care services has been implicated in the disproportionate rate of death among ethnic minority populations with AIDS. Thus, removing the linkage between HIV testing and a visit to a provider agency such as a family planning clinic, an STD clinic or an IV drug use clinics may further exacerbate the medical emergency. After receiving an HIV home test kit result, individuals who do not have a cultural or economic history of regular use of medical services may well stay away from those environments where they would have to confront the fears and stigma of AIDS.

Home Test Kits: The Fallacies

To a very large extent there are several major fallacies which undergird any proposed promotion of the AIDS home test kits. The major problem is that in each case the argument initially advanced may, on the surface, appear to address legitimate needs. But scratch the surface and the problem is much more complex.

In a major way the firms promoting the home test kit are banking on the fear of the social and economic stigma of AIDS. It is argued that home test kits may protect the anonymity of persons who are too afraid to get an HIV test because of the stigma and discrimination related to AIDS. According to this line of reasoning, the home test kit may encourage persons who otherwise might not test to find out their status. This same approach would inhibit the public health system from educating and counseling infected persons about the ways to prevent further transmission and change high risk behaviors.

This approach also presents problems from the health care perspective: if the infected individual is too afraid to interact with the health care system in order to get tested, what is going to insure that the same individual with a home test kit result will interact with the health care system to protect their health and prevent further deterioration of the immune system? The real issue is AIDS-related discrimination and the lack of confidentiality of test results. This discrimination has fueled a second epidemic of fear and prevented many at-risk individuals from obtaining an

HIV test. . Only with the enactment of broad and strong anti-discrimination and confidentiality legislation will we have effectively address the problems of the fear of disclosure to health care providers.

Another argument advanced by home test kit advocates is the lack of access to testing sites, particularly for rural Americans. According to this argument, this situation demands greater access to tools such as home test kits. While a very real question exists about the value of increasing the availability of testing devices of uncertain validity in a low risk population, thereby raising the specter of high rates of false positive test results, the real issue is access. If rural Americans do not have access to appropriate levels of AIDS-related health care, the answer is not to provide them with a substandard alternative but to make the existing service delivery system extend to reach isolated populations through the expansion of programs like the anonymous AIDS testing programs.

Finally, the proposition that somehow AIDS testing should be made easier is quite dangerous. The AIDS antibody test is a very serious matter. It provides an indication whether an individual is infected with a virus that can cause a deadly disease, that the person is probably infected for life and that the person is contagious. This kind of information is not to be treated lightly. An individual must have some kind of social support system to sustain such news. If no support system exists, then the health care personnel administering the test must provide some modicum of support through the counseling process. Otherwise we are left with individuals

learning virtually life and death news on the other end of a cold telephone line.

Thank you for the opportunity to testify. I will be happy to answer any questions.

TESTIMONY OF

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and

Deputy Director of

Center for the Biopsychosocial Study of AIDS

Department of Psychiatry

University of Miami School of Medicine

on Behalf of

THE AMERICAN PSYCHOLOGICAL ASSOCIATION

before the

The House Small Business Committee, Regulation,
Business Opportunities and Energy Subcommittee

on the Subject of

THE SAFETY AND EFFICACY OF AIDS HOME TEST KITS

AS A TOOL FOR BEHAVIOR CHANGE

I am Jose Szapocznik, Professor of Psychiatry and Deputy Director of the Center for the Biopsychosocial Study of AIDS. I am also the Director of the Spanish Family Guidance Center and of the Miami World Health Organization Collaborating Center for Mental Health and Drug Dependence, all at the University of Miami School of Medicine.

I am a member of the Congressionally mandated AIDS Program Advisory Committee to the Secretary of the Department of Health and Human Services and to the Director of the National Institutes of Health, and a member of the AIDS Policy Subcommittee of the National Advisory Council on Mental Health of the National Institute of Mental Health.

I testify as a member of the American Psychological Association representing its 90,000 members involved in all aspects of HIV and AIDS related work: from scientists designing more effective public health strategies for slowing the spread of the epidemic to those attempting to slow the progress of HIV disease by unraveling the mysteries of psychoneuroimmunology; From psychotherapists working to change individuals' unsafe, high risk behaviors to those caring for the casualties of the epidemic and their significant others. As a behavioral scientist, my objective is to summarize and interpret the available evidence that might be relevant to the use of AIDS home test kits as a tool for promoting changes toward safer behaviors.

The primary purpose of my testimony, then, is to address the safety and efficacy of HIV antibody home testing kits as an

instrument for changing the unsafe behaviors that place individuals at risk for contracting the HIV virus. With regard to efficacy, I am not aware of any studies investigating the efficacy of AIDS home test

kits in bringing about changes in unsafe or risky behaviors.

In general, the value of testing alone has been found to be highly questionable. Relevant data (Coalition, 1989) has been obtained from individuals who were screened out from enlistment with the military due to their HIV positive status. Interpretation of positive results and counseling were not provided to these individuals. A follow up survey revealed that these seropositive individuals continued to engage in high risk behaviors. Hence testing alone did not result in safer behaviors. Thus we would be in very strong grounds to state categorically that the efficacy of the procedure under discussion has not been established. The burden of proof that AIDS home test kits would result in reductions of unsafe risky behavior clearly rests with those who are attempting to make such a claim (cf. Institute, 1989).

Not having established efficacy, our primary concern must then turn to issues of safety. In this regard we have a number of studies that while not conclusive, would suggest that HIV antibody testing without counseling may be detrimental in several respects. There are two different ways in which HIV antibody testing can be detrimental: One, it may actually encourage rather than discourage unsafe and risky behavior; and, two it may have deleterious psychological and biological effects on

individuals who find out that they are HIV positive.

Social psychologists (Perloff, 1987; Perloff & Fetzger, 1986) know that some individuals have a great capacity to perceive themselves as uniquely invulnerable to the negative consequences of external events. This is particularly the case for individuals who tend to engage in high risk behavior such as adolescents and drug abusers. Cognitive psychologists have been keenly aware of the power of selective attention: Individuals who perceive themselves as invulnerable are likely to extract from a situation the evidence that would further support their beliefs of invulnerability.

Imagine then, an adolescent who has recently engaged in unsafe sexual behavior or an intravenous drug user that has recently engaged in unsafe needle sharing. Without adequate guidance and counseling, these individuals, using an AIDS Home test kit, test themselves at home and find themselves to be antibody negative. The facts are that they have been very lucky in their game of Russian Roulette. Unfortunately, without adequate guidance and counseling, these individuals are likely to attend selectively to the factors that may have contributed to their remaining HIV negative. Their belief in their unique invulnerability, rather than being challenged through counseling, has been confirmed by the results of an AIDS Home Test Kit. We should then expect that these individuals will not only continue to engage in unsafe behaviors in the future, but will also be far more difficult to persuade in the future about the error of their beliefs. Perhaps even more tragic is the case of an individual

who engages in unsafe behaviors, tests him or herself shortly thereafter with their AIDS Home Kit to find they are seronegative, goes home and continues to have unsafe sex with their partner, all along not understanding that after exposure and infection it may take weeks or months for the AIDS test to show positive.

The second concern about the safety of HIV antibody testing without counseling concerns the detrimental effects, both psychological and biological, that result from learning of one's seropositivity. Professors Mary Ann Fletcher and Neil Schneiderman (Antoni, Schneiderman, Fletcher, Goldstein, LaPerriere & Ironson, in preparation; Laperriere, Schneiderman, Antoni & Fletcher, in preparation) of our Center have conducted a carefully and cleverly designed study in which they randomly assigned individuals who did not know their HIV status either to a psychosocial stress reduction intervention or to a control condition in which no psychosocial intervention was provided, but only the usual antibody testing counseling. For those subjects who turned out to be positive, there were critically important differences in how they responded to the news of their seropositivity according to whether or not they had been involved in some kind of a psychosocial, stress reduction intervention. Those persons who were positive and received only the minimum antibody counseling showed high levels of psychological discomfort as measured by anxiety, confusion and depression. More importantly, these persons also showed substantial impairments in their immune functioning. In comparison, the

individuals who in addition to the usual HIV antibody counseling had also participated in a psychosocial, stress reduction intervention before, during and after the period of time when they received the news of their seropositivity showed far better psychological adjustment and immunologic results. These findings have important implications for a new, but rapidly developing field known as psychoneuroimmunology. According to the findings in this field, psychosocial adjustment has a direct impact on immune function. Hence, we have to realize that helping an individual cope effectively through counseling with the news that they are HIV positive will not only improve their psychological adjustment, but will also have a beneficial health outcome.

To summarize, thus far we have discussed the lack of available information on the efficacy of AIDS Home Test kits as a procedure for changing high risk behavior. We have also presented evidence that suggests that AIDS Home Test Kits without adequate counseling may actually have the reverse of the desired effect in individuals who may have an erroneous belief in their invulnerability; and we have also suggested that the minimal amount of counseling that is now provided may not be enough to ward off some of the more subtle psychological and biological negative impacts of learning that one is seropositive. Hence, we would suggest that a more comprehensive psychosocial intervention package than the minimal that is now required may be desirable.

I would now like to turn your attention to another area that

perhaps should receive much more attention and support. While there is no demonstrated efficacy of AIDS home test kits, there is evidence for the efficacy of other behavioral strategies in changing unsafe risky behaviors. Working with homosexual and bisexual men, for example, researchers at the University of California in San Francisco have demonstrated that education and prevention campaigns have resulted in profound modifications of unsafe sexual behaviors (Stall, Coates, & Hoff, 1988). These results are among the most powerful effects ever recorded in any campaign to change health related behaviors. For those individuals who may not respond to broad community education models, more intensive interventions may be required and some such interventions have been found to be highly effective in changing unsafe risky behavior among homosexual and bisexual men. One such effort (Valdiserri, Lyter, Leviton, Callahan, Kingsley & Rinaldo, 1989) demonstrated that for people to change their unsafe behavior they may require skills training that will teach them how to perform the activities that will protect them from infection. For women, skills training such as assertiveness training may be particularly needed, since for women safe sex requires that they prevail over their sexual partners (Cochran & Mays, 1989). For intravenous drug users, perhaps one of the most difficult populations to change, according to Dr. Charles Schuster (Schuster, 1988), Director of the National Institute on Drug Abuse, studies increasingly demonstrate that many IV drug users are capable of changing their unsafe behaviors. The best recognized authority in the field, Don Des Jarlais (Des Jarlais &

Friedman, 1988) concluded in 1988 that more than half of intravenous drug users that have participated in the behavior change studies he has reviewed in fact changed their unsafe behavior. However, in the case of intravenous drug users, few change their behavior as a result of information alone. Intravenous drug users tended to change their unsafe behaviors when alternatives to unsafe behaviors were available. In our own Center at the University of Miami (Page, Smith, Kane & Morgan, in preparation) exciting breakthroughs are being achieved in developing a better understanding as well as a technology of change for work with intravenous drug users.

Clearly, a whole range of behavior change strategies are required beyond simple AIDS testing. These strategies range from education for the most psychologically accessible populations to counseling, skills training and provision of alternatives to unsafe behaviors. Considerable more work is needed in reaching out to populations that are difficult to change, and in designing more intensive counseling interventions for these groups.

I would like to close my remarks to this distinguished body by addressing directly some of the arguments put forth by those who advocate AIDS Home Test Kits. One argument has been that some persons may not seek testing at alternative test sites. Yet, in a study of alternative test sites, scientists found (Kegeles, Catania and Coates, 1988) that nearly half of the heterosexuals seeking testing had engaged in unsafe sex in the past month, and over one half of the intravenous drug users seeking testing had engaged in unsafe needle sharing in the past

month. Hence, alternative testing sites are magnets, attracting the kind of populations that continue to engage in unsafe behavior, and which through counseling, skills development or the provision of alternatives to unsafe drug use, we may be able to change. If AIDS Home Test Kits become available, we may lose the golden opportunity to attract these individuals to whatever proven and effective behavior change strategies we do have.

It would be helpful to remind ourselves that the ultimate goal of our public health efforts is to prevent the transmission of HIV. This requires that individuals refrain from engaging in unsafe behaviors likely to transmit HIV to others. We now have a number of behavior change strategies that have been proven effective in altering unsafe behaviors. In the face of such evidence, it is certainly unwise and possibly even irresponsible to bring to market a procedure that has not proved efficacious, and in our judgment appears to be unsafe.

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Psychoneuroimmunology and HIV-1

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Abstract

Recent psychoneuroimmunologic findings suggest that it may be useful to evaluate the influence of behavioral factors on immune functioning and disease progression among Human Immunodeficiency Virus (HIV-1) infected individuals. Behavioral interventions with immunomodulatory capabilities may help restore competence and thereby arrest HIV-1 disease promotion at the earliest stages of the infectious continuum. We present evidence describing benefits of behavioral interventions such as aerobic exercise training on both psychological and immunological functioning among high risk HIV-1 seronegative and very early stage seropositive gay males. The HIV-1 infection is cast as a chronic disease for which early immunomodulatory behavioral interventions may have important physical and psychological impact.

PSYCHONEUROIMMUNOLOGY AND HIV-1

The etiologic agent of acquired immune deficiency syndrome (AIDS), is the human immunodeficiency virus (HIV-1), a retrovirus of the human T-cell leukemia/lymphoma line (HTLV-III family). Although AIDS is a devastating disease that has reached epidemic proportions, its effects upon the immune system provide a "natural laboratory" for studying the relationships among behavior, immunomodulation, and immune-related disease processes.

A unique feature of HIV-1 infection is that it can have a long asymptomatic phase that may last as long as 10-15 years (Munoz, Wang, Good et al., 1988). During the asymptomatic phase the individual is capable of transmitting this disease (Stevens, Taylor, Zang et al., 1986) and immune functioning is compromised (Fletcher, Caralis, Laperriere et al., 1988). Because the HIV-1 infected individual typically goes through several stages of progressive quantitative and qualitative decrements in immunological functioning that may be associated with disease progression over an extended period of time, the HIV-1 syndrome should be viewed as a chronic disease. As HIV-1 disease progresses, a loss in overall immunocompetence leaves HIV-1-infected individuals susceptible to opportunistic infections, which most commonly include pneumocystis carinii pneumonia, cryptococcal meningitis, toxoplasmosis, candidiasis, and herpes simplex (Kaplan, Wofsky, & Volberding, 1987).

The relationships among behavior, immunological functioning and HIV-1 progression are not yet understood, but there is reason to believe that such relationships may exist. First, there is a growing literature relating natural (Glaser, Rice, Sheridan et al., 1987; Irwin, Daniels, & Bloom, 1987; Kiecolt-Glaser, Fisher, Ogrocki et al., 1987; Patterson, Grant, & McClurg, 1986) and experimentally-induced stressors (Borysenko & Borysenko, 1982; Monjan & Collector, 1977; Shavit & Martin, 1987) to changes in immune function. Second, several psychological variables including mental depression (Calabrese, Skwerer, & Barna, 1986; Kiecolt-Glaser, Garner, Speicher et al., 1984; Schleifer, Keller, Siris et al., 1985), perceived loss of control and feelings of helplessness (Baum, McKinnon, & Silva, 1987; Rodin, 1988) have also been associated with altered immune functioning. Third, suggestive evidence has accrued associating psychosocial stress with the progression of HIV-1 infections (Coates, Temoshok, & Mandel, 1984; Cecchi,

1984; Donloup, Wolcott, Gottlieb et al., 1985; Solomon & Temoshok, 1987) and putative mechanisms have been offered to explain these associations including stressor-triggered activation of latent HTLV-III virus to a vigorous replicating state (Sodroski, Rosen, & Haseltine, 1984, cited in Solomon, 1987; Glaser & Kiecolt-Glaser, 1987). Fourth, we have observed that both the anticipation and the impact of being told their HIV-1 antibody status influences immune function in seronegative gay males (Ironson, O'Hearn, Laperriere et al., 1988). Fifth, we have seen some evidence of immune enhancement in HIV-1 seronegative and seropositive individuals who have undergone a 10 week aerobic exercise training program (Laperriere, O'Hearn, Ironson et al., 1988). In view of the current status of psychoneuroimmunologic research, there is reason to raise the possibility that behavioral factors may influence immune function in victims of HIV-1 disease and that behavioral interventions (e.g., aerobic exercise, stress-management, relaxation training) may provide some benefit especially during the early stages of this chronic disease.

Immune Function and HIV-1

The Center for Disease Control (CDC) lists several stages of HIV-1 infection: CDC₀ = no infection; CDC₁ = asymptomatic HIV-1 infection is present; CDC₂ = lymphadenopathy present; CDC₃ = early AIDS-Related-Complex (ARC); and CDC₄ = (severe ARC) AIDS (CDC, 1987).

As previously mentioned, the length of the asymptomatic phase of HIV-1 infection can be quite long, perhaps as long as 10-15 years in some cases (Munoz, Wang, Good et al., 1988). Five years after seroconversion to HIV-1 status in homosexual men, only 20% of 1523 infected individuals developed AIDS. This study found that AIDS is unlikely to develop before 12 months after seroconversion, that an increasing incidence of AIDS is present between 12 and 30 months, and that the incidence rate remained constant between 30 and 60 months.

The profile of immunologic abnormalities found in AIDS patients is quite heterogeneous in nature, as cell-mediated (T-cell), humoral (B-cell), and natural immunity (monocyte and natural killer [NK] cell) are affected. The primary target of HIV-1 is the T-helper/inducer cell (CD₄), a subset of T cells defined by monoclonal antibodies T₄ and Leu₃ (Fauci, Macher, & Longo, 1983).

The virus attaches itself directly to a surface membrane receptor of the CD₄ cell. Once the CD₄ cell is infected, it soon dies and is lost from the circulation. In healthy individuals, the CD₄ subset comprises approximately 60% and the CD₈ subset, which includes the T-cytotoxic and suppressor cells, comprises approximately 30% of peripheral blood T cells, resulting in a CD₄ to CD₈ ratio of 2 to 1 (Fauci et al., 1983). AIDS patients have a marked quantitative deficiency of CD₄ cells with the number of CD₈ cells usually elevated, resulting in a reversal of the CD₄ to CD₈ ratio (Fletcher, Baron, Ashman et al., 1987).

AIDS patients also have profound deficiencies in the ability of CD₄ cells to signal B-cells to respond to antigenic challenge as indexed by the Pokeweed mitogen (PWM) assay (Fletcher et al., 1987). The B cells of AIDS patients are unable to respond with an augmentation of antibody (immunoglobulin) production against this mitogen. Paradoxically, AIDS patients also have a markedly hyperactive B-cell proliferative response, resulting in abnormally high levels of secreted immunoglobulins (Igs), which are undirected and rather non-specific in action against the virus (Lane, Masur, & Edgar, 1983). Moreover, AIDS patients are deficient in their ability to mount an antibody response to in-vivo immunization with a novel antigen (Lane et al., 1983). In sum, the humoral immune system in AIDS is no longer operating in an optimal manner, since normal signals and feedback mechanisms from T cells have been altered.

Monocytes, the cells that present an antigen to T cells, are also infected by HIV-1 through a cell surface CD₄ receptor (LeSane, Gardner, Popovic et al., 1988). However, unlike the CD₄ cells, monocytes are not killed by the virus and they may propagate HIV-1 at low levels for a long period of time (Poli, Wilson, Folks et al., 1988). The monocytes remain in circulation as virtual storehouses for the virus. The number of monocytes increases in early HIV-1 infection (Fletcher et al., 1988) and in AIDS, which may be detrimental since infected monocytes act as "viral manufacturing plants" appearing to take over the genetic machinery of the monocyte. Furthermore, HIV-1 infection is associated with defects in monocyte functioning which include: defective chemotaxis; muted ability to kill certain target cells such as parasites; and decrements in their ability

to produce Interleukin-I (IL-1) in response to usual inducers of IL-1 secretion (Fauci, 1984). The compromise of these functions along with accompanying changes in other cytokine and lymphokine production, ability to kill ingested pathogens, as well as reports of altered metabolic functions required to promote intracellular killing by HIV-1 infected monocytes (Smith, Gartner, Segovic et al, 1988; Landay, Kessler, & Rothberg, 1988), may be important in terms of understanding AIDS patients' susceptibility to infections with microorganisms, such as pneumocystis carinii. Protection against these pathogens requires an intact T-cell-monocyte communication axis for mounting an effective immune response.

Another branch of the immune system (non-specific natural immunity) relevant to HIV-1 infection involves NK cells, which play an important role in immune surveillance against tumor cells and viruses. In nonspecific immunity, prior exposure to a specific antigen or Class I or Class II self-antigens are not involved in killing, in contrast to CD8 cytotoxic cells (cell-mediated immunity) which do require both prior exposure and priming plus recognition of self-histocompatibility antigens. Normal NK cytotoxicity is about 38% (Baron, Klimas, Fischl et al., 1985). This level is significantly reduced below 25% prior to HIV-1 infection in high risk groups including homosexual males and intravenous (IV) drug users (Klimas, Page, Chitwood et al., 1988) and reaches lows of 16-18% in positive IV drug users (Klimas, Blaney, Morgan et al., 1988), ARC (CDC₃) and AIDS (CDC₄) patients (Baron et al., 1985). The NK cell number is not greatly affected in any of these groups, but the cytotoxic activity has significantly declined long before the first overt symptoms of HIV-1 infection appear. This deficient NK cytotoxic response is corrected in-vitro by the addition of Interleukin-II (IL-II) to cultured cells, suggesting that the lack of signaling by the CD4 cell to the NK cell may be functionally defective (Fauci, 1984).

Blastogenesis, a measure of functional immune responsiveness by subsets of T and B cells to the mitogens Phytohaemagglutinin (PHA), PWM, Concanavalin A (ConA) and Staphylococcus Aureus, is decreased in early HIV-1 infection and is greatly depressed as the infection progresses to ARC and AIDS. Baseline immunological profiles from our ongoing longitudinal study of 22 HIV-1 seropositive homosexual males (CDC-1) indicate that even before any physical

symptomatology associated with HIV-1 infection emerges, blastogenesis via PHA declined to a mean stimulation index of 85.51 as compared to a mean PHA stimulation index of 237.75 noted among 34 HIV-1 seronegative homosexual males. Similarly, the mean PWM stimulation index in these HIV-1 seropositive men declined to 6.17 as compared to HIV-1 seronegative men with a mean PWM index of 13.52 (Fletcher et al., 1988). These results suggest that among asymptomatic seropositive individuals, the humoral immune response to antigens has already been adversely affected, perhaps leaving individuals of such groups more susceptible to other infections long before the physical signs of HIV-1 become noticeable.

The common underlying immunological defect among the T cells, B cells, monocytes, and NK cells in AIDS patients appears to result from a "domino effect" as the primary HIV-1 target cells, the CD4 cells, are rendered non-functional, preventing the normal signaling that is essential for further immune mobilization and adequate cellular and humoral immune responsiveness. Natural immune function is also negatively impacted, preventing monocytes and NK cells from providing the essential immune surveillance against parasites, tumor cells, and other pathogens. The inability of NK cells, monocytes, and CD4 cells to produce normal levels of the essential immunomodulators, gamma interferon, IL-I, and IL-II, respectively, causes a break in the chain of immune system communication. This loss of cell-to-cell signaling may be a primary factor in the loss of overall immunocompetence, leaving HIV-1-infected individuals susceptible to opportunistic infections.

The apparent abnormalities in immunological functioning seen in high risk HIV-1 seronegative individuals and the continued decline in very early stage seropositive individuals, points to the importance of early immunomodulatory interventions which may help restore competence and arrest HIV-1 disease promotion at an early stage in the HIV-1 infectious continuum. Perhaps, at this early stage of HIV-1 infection, the apparent sluggishness in immune system functioning may be most amenable to psychosocial interventions, which may help to boost signaling between CD4 cells, monocytes, NK cells, and B cells via increases in cytokine and lymphokine production. The reduction of burdening psychosocial stressors has already been demonstrated to have a positive impact on immune system functioning (Kiecolt-Glaser, Glaser, Strain et al., 1986).

Stress Hormones, Immune Function and HIV-1

The exact functional relations among behavior, immune function and HIV-1 progression are unknown. Relationships between various neurohormones and immune function have been sufficiently established to permit the advancement of hypotheses relating psychosocial variables on the one hand and immune suppression or enhancement on the other.

An individual's perception of a stressor and/or the availability or unavailability of a coping response to that stressor may trigger a series of physiological events leading to specific autonomic nervous system (ANS), neuroendocrine and neuropeptide changes (McCabe & Schneiderman, 1985). A specific pattern of ANS activation, which occurs when coping responses are available and potentially adequate to meet stressful demands, is often associated with active coping. The sympathoadrenomedullary system, activated during such active coping episodes, releases norepinephrine (NE) and epinephrine (E), which prepares the organism for stressor confrontation. Another physiological pattern appears to be dominant when coping responses are unavailable, as in those stressful situations defined as unpredictable, uncontrollable, and/or unrelenting. This pattern, associated with hypervigilance, lack of adequate coping resources, and conservation-withdrawal, is believed to be characterized by behavioral inhibition and activation of the hypothalamico-pituitary adrenocortical system (HPAC). Activation of the HPAC system is associated with adrenocorticotropin hormone (ACTH) and cortisol release following signalling by corticotropin releasing factor (CRF) (McCabe & Schneiderman, 1985).

Preliminary findings suggest that elevations in CRF, ACTH, cortisol, NE, and E may be accompanied by decrements in immune function. Corticotropin releasing factor has been shown to inhibit human NK cytotoxic activity and may do so by stimulating cyclic AMP (cAMP) in large granular lymphocytes (Pawlikowski, Zelazowski, Dohler et al., 1988). This finding is significant in that CRF release from the parvocellular nucleus of the hypothalamus is the initiation step in HPAC activation (McCabe & Schneiderman, 1985). Downstream HPAC products (i.e., ACTH, cortisol) appear to be important as well. Physiologic doses of ACTH have been shown to impair the responsiveness of T cells to antigenic (CD3 antibody) and mitogenic (ConA) stimuli and may do

so by interfering with intracellular levels of calcium, an important second messenger for T cell activation (Kavelaars, Ballieux, & Heijnen, 1988). ACTH receptors have previously been identified on lymphocytes (Bost, Smith, Wear et al., 1987, cited in Kavelaars et al., 1988). Evidence has accumulated which indicates that adrenal cortical hormones directly impair or modify several components of cellular immunity including T-lymphocytes (Cupps & Fauci, 1982; Felten, Felten, Carlson et al., 1985), macrophages (Monjan, 1981; Hall & Goldstein, 1981; Pavlidis & Chirigos, 1980), and NK cell activity (Herberman & Holden, 1978; Levy, Herberman, Lippman et al., 1987). Corticosteroids are also known to inhibit both humoral and cellular responses to several antigens (e.g., tetanus toxoid) (Stites, Stobo, Fudenberg et al., 1982) and these suppressive effects include: decreases in T cell subpopulations (Cupps & Fauci, 1982); decreased production of macrophage mitogenic factor, chemotactic factor, and macrophage migration inhibitory factor (Duncan, Sadlik, & Hadden, 1982); and impaired production of IL-1 and plasminogen activator by monocytes (Cupps & Fauci, 1982). Further, corticosteroids appear to decrease leukocyte migration-inhibition factor production in response to PHA (Hahn, Levin, & Handzel, 1976); impair NK cell activity and gamma-interferon production (Stites, Stobo, Fudenberg et al., 1982); and diminish lymphotoxin release by lymphocytes (Cupps & Fauci, 1982). Cortisol receptors have been established on lymphocytes and the interaction of these receptors with the appropriate cortisol levels may inhibit cellular immune responses via changes in DNA and RNA synthesis and uptake (see Antoni, 1987 for review). Hence, the literature supports the notion that elevated levels of cortisol are associated with impaired immune system functioning and accompanying depression of lymphokine production.

Elevations in peripheral catecholamines have also been shown to depress immune functioning ostensibly via β -adrenergic receptors on lymphocytes (Felten, Felten, Carlson et al., 1985; Hatfield, Petersen, & DiMicco, 1986; Livnat, Felten, Carlson et al., 1985; Plaut, 1987; Hadden, 1987). Sympathetic noradrenergic fibers innervate both the vasculature and parenchymal regions of lymphocytes and associated cells in several lymphoid organs where NE terminals are generally directed into zones of T-lymphocytes (Felten, Felten, Carlson et al., 1985). The administration of

β -adrenergic agonists has been associated with decreases in mouse and human NK cell killing activity and decreased T-lymphocyte proliferation, and these effects appear to be mediated by increases in intracellular cAMP levels (Plaut, 1987; Katz, Zeytoun, & Fauci, 1982).

In-vivo human studies involving infusion of adrenergic agents have shown a decrease in leukocyte number and decreased lymphocyte proliferative response to mitogens following administration of E (Livnat, Felten, Carlson et al., 1985; Crary, Borysenko, Sutherland et al., 1983). Again, these immunomodulatory effects are believed to be mediated by cyclic nucleotide action. Other work indicates that agents such as isoproterenol and prostaglandin E, which increase lymphocyte cAMP, can impair lymphocyte proliferation and killing of target cells whereas agents such as carbamylcholine, which increase lymphocyte cyclic GMP levels, enhance lymphocyte proliferative and killing abilities (Livnat, Felten, Carlson et al., 1985).

In sum, evidence exists for immunomodulatory effects of ANS and neuroendocrine agents on several aspects of cellular immunity including lymphocyte and NK cell functioning. In contrast to the actions of catecholamines and corticosteroids, pituitary and adrenal peptide stress hormones such as met-enkephalin, β -endorphin, and substance P have been shown to stimulate T-cell and NK cell responses (Mathews, Froelich, Sibbit et al., 1983; Mandler, Biddison, Mander et al., 1986; Kusnecov, Husband, King et al., 1987; Hadden, 1987; Williamson, Knight, Lightman et al., 1987), and γ -interferon production (Brown & Van Epps, 1986), as well as macrophage functioning (for review, see Sibinga & Goldstein, 1988). The fact that the synthesis and release of β -endorphin is inhibited by glucocorticoids may provide a further immunosuppressive role for substances such as cortisol (Simantov, 1979).

Recent studies have related neurohormones and neuropeptides to HIV-1 disease. One study, for example, noted that the ability of HIV-1 to infect normal human lymphocytes is enhanced by supplementing the cell culture medium with corticosteroids (Markham, Salahuddin, Veren et al., 1986). This study suggests that adrenal stress hormones may affect the susceptibility of high risk hosts to AIDS related phenomena following viral inoculation. Viral susceptibility may be related to

the efficacy of lymphocyte or NK cytotoxic abilities which may be compromised by glucocorticoid secretions during stress. In a second study, another stress-associated hormone, met-enkephalin, was shown to enhance T-cell populations in AIDS patients with Kaposi's sarcoma (Plotnikoff, Wybran, Nimeh et al., 1986). In a third study of seven ARC patients treated with met-enkephalin three times per week for 21 days, the following immunological changes occurred across the three week period: increases in OKT3%, OKT4 (equivalent to CD4) number, NK activity, IL-II production, and PHA mitogen response (Wybran, Schandene, Van Vooren et al., 1987). These investigators have also noted impressive improvements in mitogen responsivity and recession of Kaposi's sarcoma lesions in AIDS patients treated with met-enkephalin (Wybran & Schandene, 1986, cited in Wybran et al., 1987). Others have noted that the most dramatic cellular

immunoenhancing effects for opioid peptides such as met-enkephalin and β -endorphin are found in patients possessing low baseline immune functioning levels (Plotnikoff, Murgu, Miller et al., 1985; Fontana, Fattorossi, D'Amelio et al., 1987). All of this work must be viewed, however, as preliminary, considering the small sample sizes, and lack of replication across laboratories.

Psychosocial Stressors, Immune Function and HIV-1

Several behavioral variables have been associated with altered immune functioning. Animals subjected to uncontrollable stressors, for instance, have been noted to display elevated plasma corticosteroids and depleted brain NE levels (Weiss, 1982 cited in McCabe & Schneiderman, 1985; Pericic, Manev, Boranic et al., 1987), and increased peripheral catecholamine release (Mason, 1975), as well as immune system decrements such as thymic involution (Selye, 1976), decreased NK cell cytotoxicity (Shavit, Lewis, Terman et al., 1984; Shavit & Martin, 1987; Shavit, Martin, Yirmiya et al., 1987), suppressed lymphocyte proliferation (Laudenslager, Ryan, Drugan et al., 1983) impaired plaque-forming cell response to sheep red blood cells (Pericic, Manev, Boranic et al., 1987), and decreased helper/suppressor cell ratios (Teshima, Sogawa, Kihara et al., 1987).

Research using naturally occurring uncontrollable stressors, in human subjects, has identified some parallels to the animal findings noted above. Much of this has been reviewed elsewhere (Antoni, Schneiderman, Laperriere et al., in press). The experience of chronic environmental

stressors characterized by a loss of personal control (e.g., being a resident of Three-Mile Island during the nuclear reactor accident) among normal healthy subjects was accompanied by increased symptoms of psychological distress (e.g., anxiety, depression); elevations in urinary catecholamine levels; and decreases in total T-lymphocyte number, total macrophage number, and total number of CD4 cells (Baum et al., 1987). In recent work with a geriatric population in which the effects of perceived controllable vs. uncontrollable major stressful events were evaluated for immunomodulatory effects, uncontrollable events were associated with decrements in CD4/CD8 ratios and PHA mitogen response (Rodin, 1988).

Social stressors have been associated with elevations in stress hormone levels and impaired immune functioning in the animal and human literature. Animal models of separation stress and social isolation in monkeys and social isolation/population density manipulations in mice have yielded reliable hormonal and immunomodulatory effects. For example, infant monkeys separated from their mothers show a behavioral response suggesting depression and helplessness (Coe, Wiener, Rosenberg et al., 1984, cited in Lloyd, 1987), elevated cortisol levels (Coe & Levine, 1981), and compromised immune functioning (Coe et al., 1984, cited in Lloyd, 1987). Social stressors most commonly associated with glucocorticoid elevations and cellular immunomodulation (NK activity, mitogen responsivity) in human work include loneliness (Kiecolt-Glaser, Ricker, George et al., 1984), marital disruption (Kiecolt-Glaser, Fisher, Ogrocki et al., 1987), lack of social support networks (Levy, Herberman, Maluish et al., 1985; Levy, Herberman, Lippman et al., 1987), and bereavement (Irwin, Daniels, & Weiner, 1987; Calabrese, Kling, & Gold, 1987; Kosten, Jacobs, & Mason, 1984). Regarding physiological mediation, it is noteworthy that 24-hr urinary catecholamine excretions of NE and E are elevated in bereaved subjects and in subjects threatened with a loss as compared to normals (Jacobs, Mason, Kosten et al., 1986).

In a series of behavioral immunology studies in which social support, mood, and NK activity were evaluated among breast cancer patients, a lack of social support predicted poorer NK activity (Levy, Herberman, Maluish et al., 1985; Levy, Herberman, Lippman et al., 1987; Levy & Herberman, 1988). Other recent work has noted that a high stress level, increased depressive

symptoms, dissatisfaction with social support, and limited use of adaptive coping strategies predicted decreased CD₄ cell number and increased CD₈ cell number among elderly women (McNaughton, Patterson, & Grant, 1988).

Clinical depression or depressed affect have been linked with impaired cellular immune functioning in numerous studies. Compared to control subjects, patients with major depressive disorder show decreased PHA and Con A responses (Kronfol, Silva, Greden et al., 1983; Calabrese, Skwerer, Barna et al., 1986; Schleifer, Keller, Siris et al., 1985) as well as lowered percentages of helper T lymphocytes (Krueger, Levy, Cathcart et al., 1984). Severity of depressive symptomatology has also been associated with diminished Con A and PHA responses (Monjan, 1987), and decreased NK activity (Kiecolt-Glaser, Garner, Speicher et al., 1984; Irwin, Daniels, & Bloom et al., 1986). Depressive symptoms were predictive of decrements in NK activity among women when measured before and after the death of their husbands (Irwin, Daniels, Smith et al., 1987).

Anxiety and depression are common sequelae to the diagnosis of HIV-1 infection and may vary somewhat over the course of the disease (Goodkin, 1988; Tross, 1987). It is noteworthy, for example, that ARC patients appear to be more distressed than AIDS patients (Temoshok, Zich, Mandel et al., 1986; Tross, Hirsch, Rabkin et al., 1987). Tross (1987) attributes these differences to the greater degree of uncertainty in the lives of the ARC patients. In any event, the existing literature showing that depressive symptomatology impacts upon the immune system raises the possibility that psychological factors (i.e., anticipation and impact of a seropositivity diagnosis) might exacerbate the immune suppression induced by the HIV-1 infection. The nature of this interaction may also be expected to vary at different stages of the disease process. During the past 2.5 years we have been studying relationships among behavioral factors, psychological functioning and immune responses in high risk gay males just before and after they receive their HIV-1 diagnoses. We have also begun to examine the effects of behavioral interventions aimed at enhancing psychologic and immune functioning in these asymptomatic antibody HIV-1 positive and negative gay males.

Miami Asymptomatic HIV-1 Project

Our current work at the University of Miami involves the investigation of psychological and immunological functioning among asymptomatic gay males across the "anticipatory" period preceding their HIV-1 antibody testing and during the "impact" period following news of their antibody status. Further, we have studied the effects of stress management intervention techniques (e.g., aerobic exercise, cognitive stress management, relaxation training) on immune functioning in gay males who are unaware of their HIV-1 status at entry. The stress management interventions are employed in two experimental groups: an aerobic exercise group and a psychosocial intervention (relaxation training plus cognitive stress management) group. Several biological, psychological, and social outcome measures are compared between the two experimental groups and between each of the experimental groups and a no contact control group. Each group manipulation, to be described below, comprises an intervention conducted either two or three times weekly (total time = 135 min/wk) across a 10-week period in groups of four to six subjects.

Because we are especially interested in individuals at the earliest stage of HIV-1 infection, the study sample includes gay males meeting the following exclusionary criteria: 1) having a diagnosis of AIDS or ARC; 2) unexplained weight loss; 3) oral candidiasis; 4) lymphadenopathy; 5) fever of unexplained origin; or 6) unexplained night sweats, or diarrhea. In addition we have excluded subjects who report drug or ethanol abuse, use of anabolic steroids, regular use of anti-histamines, are under 18 years of age, or who are participating in a regular physical exercise or meditation regimen.

Across the duration of the 10-week experimental manipulation and a 48-month follow-up period, several batteries of biological, psychological, and social measures are collected. These measures provide: baseline data; outcome status immediately before and after knowledge of HIV-1 diagnostic status is communicated to subjects; status at one-week, three-weeks, and three-months post HIV-1 testing; and outcome at four 12-month follow-up intervals. This schedule allows us to assess several variables for pretreatment levels, early treatment effects, stress-buffering treatment

effects (stressor = diagnostic test results), posttreatment effects, and follow-up (carry over; treatment-generalizability effects).

Biological outcome measures include immunological, endocrine, and neuropeptide levels assessed at the time points noted previously. Cellular immune measures include total T cells, B cells, and T-helper/suppressor cell ratio; coexpression and antigen density surface markers for T cell activation markers, T-helper cell subsets, NK cells and NK cell subsets, B cell activation markers, and monocyte activation markers; lymphocyte proliferative responses to PHA and PWM; NK cytotoxic activity; interferon and IL-II levels in the supernatants of mitogen stimulated mononuclear cells; and monocyte killing of tumor targets. Humoral factors which are measured include serum immunoglobulins (IgG, IgA, and IgM), Forssman antibody (measures transient polyclonal B cell activation), Paul-Bunnell heterophile antibody, Epstein-Barr virus (EBV) antibodies, and HIV antibodies (ELISA assay plus confirmation by Western blot). The endocrine and neuropeptide measures include plasma cortisol and β -endorphin, respectively. In addition to these biological measures, nutritional status is assessed via albumin determination.

Psychological outcome measures employed in this design include several indices of coping skills/styles; cognitive/attitudinal measures (e.g., optimism, hardiness, self-efficacy); affect-based inventories (e.g., POMS, Cook-Medley scale, STAI), and behavioral measures (e.g., sexual and health behaviors). Social outcome measures consist of loneliness, social support, and sexual disclosure questionnaires.

Anticipatory Anxiety and Impact

We were first interested in assessing changes in psychological and immune functioning of asymptomatic gay males during the period between entry into the study (baseline) and HIV-1 antibody testing (week 0 to 5). Previous work has shown reliable changes in immunological and distress markers during the period preceding impending stressors such as medical school examinations (Glaser et al., 1987). We found that during the five weeks preceding news of their HIV-1 antibody status 29 gay seronegative males showed a significant enhancement in several immune parameters (Ironson, O'Hearn, Laperriere et al., 1988). These effects included increases

in: NK cell cytotoxicity, lymphocyte response to either PHA or PWM monocytes expressing class II antigen (MO_2+I_2), number of monocytes (MO_2+), and the subpopulation of CD_4 cells which activate the CD_8 cells ($2H_4+T_4+$). Within 72 hrs of receiving news of HIV-1 antibody status these seronegative subjects, however, showed a significant decrement in NK cell cytotoxicity and MO_2+ . These findings suggest that the anticipation of HIV-1 antibody status is acting as a potent stressor which mobilizes immune functioning. Following news of antibody status, these individuals appear to return to baseline levels on at least some immune measures although not PWM or PHA.

In the case of PWM the HIV-1 seropositive subjects showed approximately 1700 counts per min at baseline whereas the HIV-1 seronegative subjects revealed 4000 counts per min. It can be seen in Figure 1 that the counts per min increased in the period preceding diagnosis and reached a peak level in the first measurement period after diagnosis. This level was maintained between weeks 6 and 10 of the study. Virtually the same pattern of results was obtained for PHA (not shown).

In contrast to the seronegatives, we found that 17 HIV-1 antibody positive subjects failed to show either immune enhancement during the anticipation phase or any immune changes after receiving news of their diagnostic status, suggesting that their immune system may be compromised to such a degree that it is insensitive to psychosocial factors (i.e., anxiety). If this premise is correct, it suggests that psychosocial factors may relate to immune functioning in different ways for seropositives and seronegatives, regardless of the degree of overt symptomatology. Taken together, the results emerging from our laboratory and those noted in the recent literature provide a good empirical basis for an association between stressful experiences and changes in immune functioning among humans.

Insert Figure 1 about here

Stress Management Interventions

Immunomodulatory treatments have been proposed for HIV-1 infected individuals including interferon and azidothymidine (AZT) regimens. Although, these interventions often produce

improvements in cellular immunity (Fischl, Richman, Grieco et al., 1987) they can also have undesirable physiological (e.g., bone marrow suppression, anemia, neutropenia; Richman, Fischl, Grieco et al., 1987) and psychological (e.g., depression; Solomon & Mead, in press) side effects. Others have noted that most anti-viral drugs available would be too toxic for humans if given at sufficient doses (Goodkin, 1988).

We have operated from a chronic disease rationale that HIV-1 spectrum sequelae represent points along a continuum of manifestation of underlying immune dysfunction. In the earliest stages, HIV-1 infected individuals are asymptomatic despite showing impaired cellular immune functioning. We reasoned that stress management interventions that can enhance immune function might forestall or eliminate the onset of disease complications such as opportunistic infections and neoplasia among these individuals. Here, behavioral interventions designed to enhance relaxation and coping skills, social support, and self-efficacy may likewise enhance immune functioning and retard disease progression among early HIV-1 seropositive individuals. In previous work, relaxation training has been shown to increase NK cell activity in a geriatric sample (Kiecolt-Glaser, Glaser, Williger et al., 1985) and increase PHA and ConA mitogen responsivity, IL-II production, and NK cell activity among metastatic cancer patients (Gruber, Hall, Hersh et al., in press). It is noteworthy that the samples in both of these studies are likely to have been immunocompromised at the outset of this intervention but subsequently benefitted clinically from behavioral stress management interventions.

Another behavioral intervention with both stress attenuating and immunomodulatory effects is aerobic exercise training. Sustained improvements in aerobic fitness level during exercise training programs have been associated with increased perceptions of psychologic well-being (Morgan, 1985), reductions in anxiety (Morgan, 1984), decreases in depression (Greist, Klein, Eischens et al., 1979), and enhanced self-esteem (Morgan, 1982), as well as with increases in the percent of T-lymphocytes (Watson, Moriguchi, Jackson et al., 1986). Temoshok, Zich, Solomon et al. (1987) showed that survival time and some markers of immune functioning were associated with fitness level in HIV-1-infected males (cited in Kiecolt-Glaser & Glaser, 1988). We have

investigated the psychological and immunomodulatory effects of an aerobic training program among asymptomatic HIV-1 seropositive and seronegative gay males.

In order to demonstrate that stress management interventions have immunomodulatory effects and can delay or reduce HIV-1-related disease outbreaks we have investigated gay males at the earliest stages of the HIV-1 chronic disease process in a randomized experimental design. The two experimental groups (aerobic exercise and psychosocial intervention) are each exposed to a 10-week treatment program. In each case manipulation checks are included to assess: 1) the contribution of potential confounds (e.g., sleep, physical activity levels), and 2) compliance with and retention of the experimental manipulation. A no-contact control group comprising seronegatives and seropositives serves as the comparison group.

Aerobic exercise protocol. The aerobic exercise training protocol consists of 45 min of aerobic training (riding a bicycle ergometer) 3 times per week across the 10 week intervention period at roughly 80% of their age-predicted maximum heart rate. Manipulation check measures for treatment compliance and retention include questions relevant to the intervention of aerobic exercise training, as well as, periodic aerobic fitness evaluations. Additional questionnaires, administered at week, 1, 5, 7, 8, and 10, are included to assess the contribution of potential confounds (e.g., sleep and level of physical activity) noted in the literature (Antoni et al., in press; Kiecolt-Glaser & Glaser, 1988). For example, several questions were included to insure that the control group was not exercising on their own. These questions are verified empirically by aerobic fitness evaluations at weeks 1, 5, and 10.

The aerobic fitness evaluation, a key manipulation check, is a measure of maximal aerobic power, and yields an individual's maximum volume of oxygen consumption (VO_{2max}) (Saltin & Astrand, 1967). Our findings indicate that this experimental protocol results in a significant improvement in aerobic fitness (VO_{2max}) after 5 weeks of training among both HIV-1 antibody negative and positive subjects (Laperriere et al., 1988). This increase in aerobic fitness is maintained during the next 5 weeks and is accompanied by a significant increase in CD4 cells regardless of HIV-1 status (Laperriere, O'Hearn, Ironson et al., 1988). In addition, we have found

that HIV-1-seronegative gay males completing this 10-week training program show an increase in mature B-cells and 2H₄+T₄+ cell numbers. As mentioned previously, the 2H₄+T₄+ cell line comprises a subset of helper cells which activate CD8 cells (Laperriere et al., 1988). These studies indicate that a program of aerobic exercise training enhances certain host defense components of cellular immunity. These effects, however, appear to differ among HIV-1-infected and non-infected individuals suggesting that the integrity of the host's immune system at baseline may determine an upper limit to aerobically-induced immunomodulatory effects.

Although seropositive individuals derived fewer immunomodulatory benefits from aerobic training than seronegatives, this intervention appeared to substantially buffer the psychological impact of news of seropositivity. We found that HIV-1 seropositive controls showed marked increases in tension-anxiety (see Figure 2), depression, and confusion-bewilderment as measured by the POMS at 72 hrs post diagnosis, whereas exercisers showed significantly lower elevations on these distress indices. Given the high incidence of anxiety disorders, depression, and suicidal ideation among recently diagnosed HIV-1 infected individuals noted in several studies (Tross, 1987; Morin, Charles, & Malyon, 1984) the psychological buffering effects of our aerobic exercise training protocol appear to have profound implications. We are currently investigating the role of potential mediators (e.g., β -endorphin) to account for these psychological and immunological effects. Hence, our preliminary findings suggest that aerobic exercise training may offer significant psychological and immunological benefits for HIV-1-infected individuals who are at very early stages of this disease process. Our longitudinal data will allow us to assess the impact of this intervention on HIV-1 associated physical (e.g., opportunistic infections) and psychological (e.g., anxiety) sequelae across a 48-month follow-up period.

 Insert Figure 2 about here

As part of our experimental design we are comparing the aerobic exercise group with a no contact control and a psychosocial stress management group. The psychosocial protocol comprises several features including progressive muscle relaxation training, mental imagery, cognitive

restructuring, assertiveness training, and social support sensitization/enrichment. Subjects receive training in progressive muscle relaxation (PMR) during one 45 min session each week and also learn other stress management techniques in a separate 90 min weekly session. This design will allow us to investigate immunological and psychological effects of psychosocial stress management techniques in comparison with exercise and control groups.

Conclusion

Human immunodeficiency virus (HIV-1) infection can be viewed as a chronic disease with clinical sequelae such as opportunistic infections and neoplasias representing points along a continuum of manifestation of underlying immune system dysfunction. In light of recent psychoneuroimmunologic findings, the possibility that behavioral factors may influence immune function among HIV-1 infected individuals seems viable. The abnormalities in immunological functioning observed in high risk HIV-1 seronegative individuals and the insidious decline in very early stage seropositive individuals, highlights the importance of early immunomodulatory interventions which may help restore competence and halt HIV-1 disease progression at an early stage in the HIV-1 infectious continuum. Indeed we have observed discrete and significant psychological and immunological changes among asymptomatic gay males across the "anticipatory" period, preceding HIV-1 antibody testing, and during the "impact" period, following news of diagnosis. Furthermore, we have noted significant benefits of behavioral interventions on psychological and immunological functioning among asymptomatic HIV-1 seropositive and seronegative gay males. On the one hand, a time-limited aerobic exercise training program appears to enhance cellular and humoral immune functioning among HIV-1 seronegatives and to a lesser extent, seropositives. On the other hand, this intervention provided profound psychological benefits for seropositives, with effects apparent as early as 72 hrs following news of their HIV-antibody status. Long term follow-up of these individuals will allow us to assess the impact of behavioral interventions on HIV-1 associated physical and psychological sequelae across a clinically meaningful longitudinal period.

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Figure 1. Change in Pokeweed mitogen (PWM) responsivity values, expressed as counts per minute (cpm), across 10-week period among HIV seropositive and seronegative gay males.

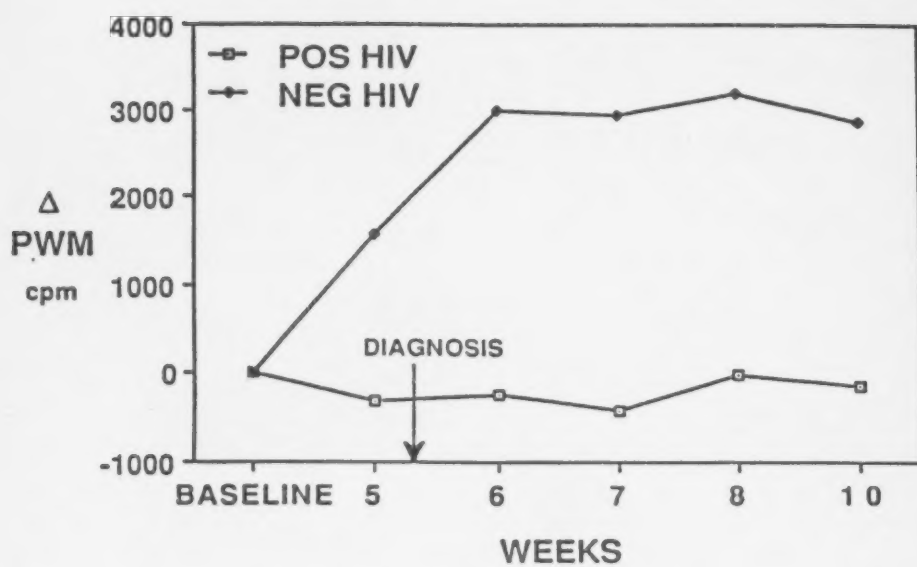
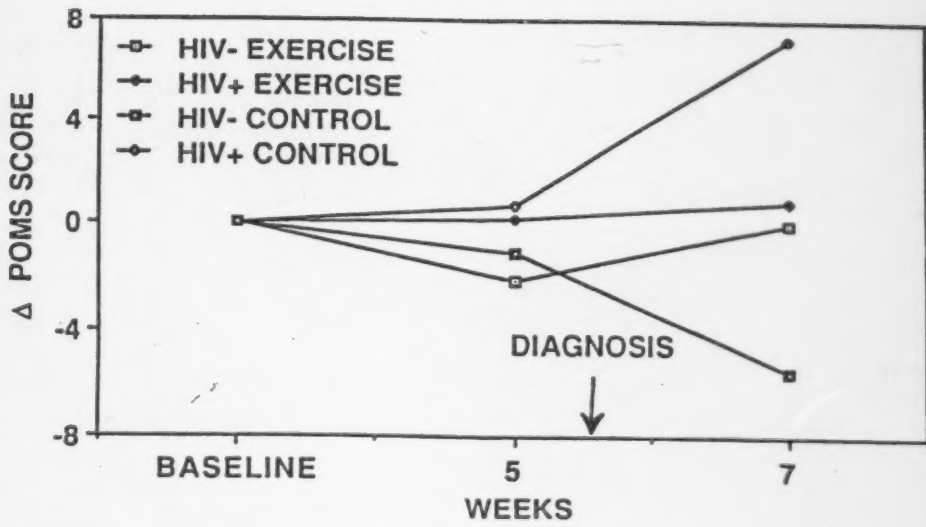
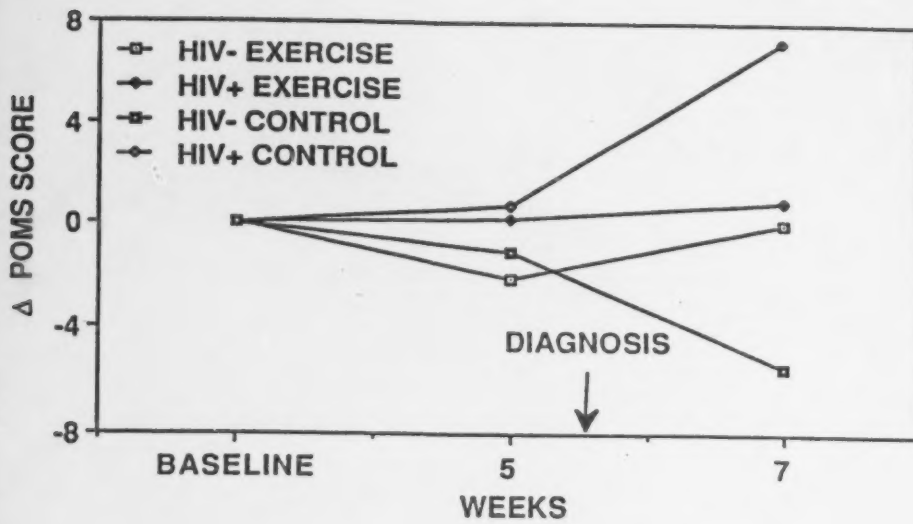
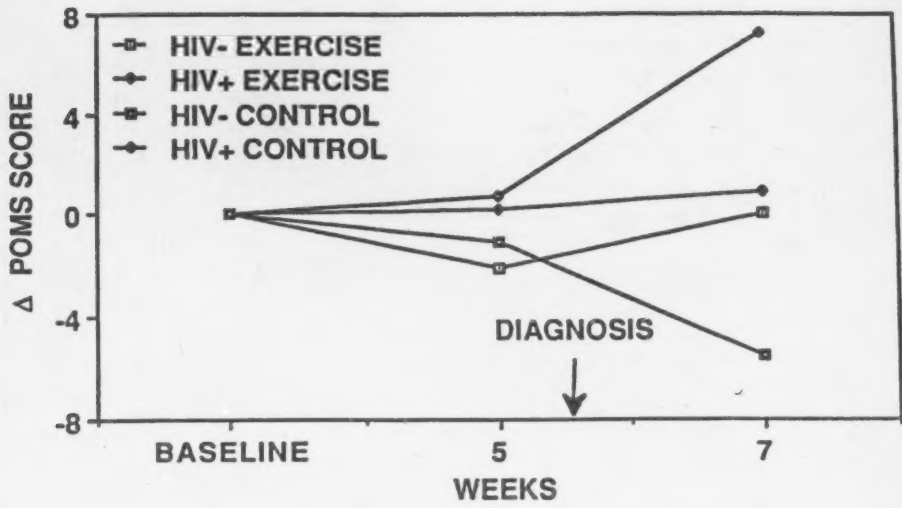
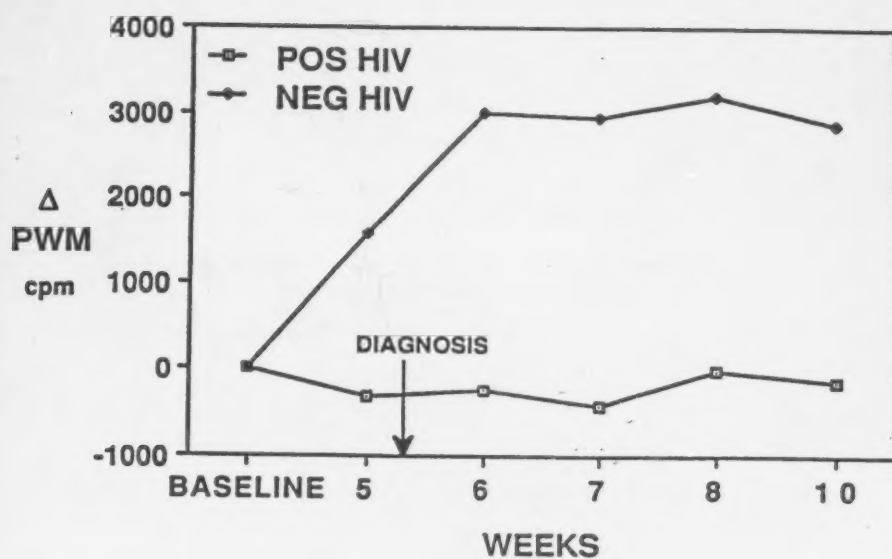


Figure 2. Change in Profile of Mood States (POMS) tension-anxiety scores from baseline to week 5 (anticipation) and from week 5 to week 7 (impact) among HIV seropositive and seronegative exercisers and controls.









TESTIMONY ON

THE U.S. AIR FORCE EXPERIENCE
WITH HIV-INFECTED PERSONNEL:
IMPLICATIONS FOR THE AIDS/HIV HOME TESTING KIT

Submitted to:

HOUSE SMALL BUSINESS COMMITTEE

Subcommittee on Regulation, Business
Opportunities, and Energy

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March 23, 1989

Mr. Chairman and members of the subcommittee; I am Major James Rundell, an assistant professor in the Department of Psychiatry at the F. Edward Hebert School of Medicine of the Uniformed Services University of the Health Sciences (USUHS) in Bethesda Maryland. I want to thank you for the opportunity to testify today on the subject of the FDA's consideration of licensing HIV home test kits. I hope these comments will shed additional light on the issue the subcommittee is discussing. Conclusions and opinions are my own and do not necessarily reflect those of USUHS, the U.S. Air Force or the Department of Defense.

All military personnel are periodically tested for evidence of infection with Human Immunodeficiency Virus, or HIV. Relevant to the issue of home test kits, notification of seropositivity is made only in person, in a medical setting, and after confirmatory tests are completed. Seropositive individuals are immediately referred to one of the military's designated medical evaluation centers for a comprehensive medical evaluation. Face-to-Face counselling and education are included. Patients receive regular and continuing medical followup from that point on.

In the Air Force, all seropositive persons are referred to Wilford Hall U.S. Air Force Medical Center in San Antonio Texas for their medical evaluations. The Department of Psychiatry there has been studying the emotional impact of knowledge of seropositivity. I'd like to tell you some of the preliminary findings from those studies that have a bearing on the issue of home test kits.

The emotional reaction to notification of HIV-seropositivity depends on a number of factors, including availability of social supports, whether there is a pre-existing psychiatric disorder such as alcoholism or depression, the amount of stigma perceived, and the biological effects of the virus on the brain. The reaction to news of seroconversion is very much individualized and complex and referral to mental health professionals is often made to sort through these complex determinants. One of the disadvantages of telephone counselling is that unless every community in the nation has a local telephone counsellor, there will not be knowledge of appropriate local referral sources that face-to-face counsellors have available.

Most HIV-seropositive persons in the Air Force's mandatory testing program adjust well. However, significant adjustment problems occur in many cases. For example, two in ten patients experience anxiety or depressed mood to a degree that causes disruptions in social or occupational function. Another one in ten will require treatment for clinical depression, frequently with antidepressant medications. Alcohol abuse occurs in at least one in ten,

probably more. Various psychiatric rating scales reveal abnormally high levels of anxiety, depressed mood, or general distress in one-third.

Suicides and suicide attempts are potential negative outcomes of a home testing program. Suicide rates in civilians with full-blown AIDS are up to 66 times that of the general population and 36 times that of individuals who are the same gender and age. Our experience with patients at early stages of HIV infection has been of the same magnitude. We have documented a suicide attempt rate at least forty times higher than that of the Air Force in general. And one patient in five admits to at least considering suicide as an option over the next year. Only rarely does a suicide attempt occur immediately after finding out about being seropositive. Most occur several months later. Long-term face-to-face followup is the best way to approach this problem; not a one-time telephone counselling session at a period of relatively low risk for suicidal behavior.

Attempts to decrease suicide and suicide attempt rates involve identification of risk factors in the population of concern. We documented six factors that distinguish suicidal HIV-seropositive persons from demographically similar nonsuicidal HIV-seropositive persons: 1) Social isolation; 2) Multiple stresses other than HIV infection; 3) Denial of symptoms; 4) Evidence of disease progression; 5) Alcohol abuse; and 6) High levels of anxiety and depression. These suicide attempt risk factors are not unique to knowledge of HIV infection but are frequently present.

Interesting comparisons can be made between individuals who have just found out they are HIV-positive and individuals who have known for one year. There is only a modest difference in the frequency of psychiatric disorders and in measures of psychological distress between the two groups. Only the degree of depression appears to decline significantly with time. I believe that not only should counselling accompany initial testing, but that followup counselling should be available. To me, the debate should not be whether to decrease the amount of counselling provided or change it to a telephone mode but how to increase both its availability and duration. Examination of visual data such as general appearance, tearfulness, facial expressions, eye contact, posture, and grooming are integral parts of a psychiatric evaluation.

Certainly there is a difference between our population and individuals who might use a home HIV test. Military personnel take the test because they are required to do so. However, no one knows who will take the Home HIV test or for what reasons. Individuals with psychiatric disorders, irrational fears, or phobias are likely to use this test in

very idiosyncratic ways. This may be a small number, but the stakes are higher than those involved with the home pregnancy test or home tests for blood in the stool. Knowledge of HIV-seropositivity is accompanied by significant amounts of psychological distress, psychiatric disorders, and suicidal thoughts and behavior.

If there is a readily available HIV test that is used by unprecedented numbers of low-risk individuals, there will be a large number of people who suddenly experience knowing they are HIV-negative. It is not at all clear that knowledge of HIV-seronegativity facilitates safer sexual behavior. We have a number of anecdotes and reports that the opposite may frequently be true. I have personally heard the phrases "Well, what I've been doing hasn't gotten me into trouble, so why change?" or "I'm not one of them, so I'm not at risk."

In summary, these findings support the reasoning behind guidelines established by medical, mental health, and government organizations. We devote a large amount of both personal and financial resources to help patients deal with the emotional consequences of knowledge of HIV infection. A sizable minority of this group of HIV-infected persons develop psychiatric disorders and require psychiatric treatment.

Once again, I thank the subcommittee for the opportunity to testify and would be glad to answer any questions.

TESTIMONY ON

**RISKS AND IMPLICATIONS
OF AIDS/HIV TESTING
IN NON-TRADITIONAL LABORATORIES
AND IN THE HOME**

submitted to

**SUBCOMMITTEE ON REGULATION,
BUSINESS OPPORTUNITIES AND ENERGY**

of the

HOUSE SMALL BUSINESS COMMITTEE

on behalf of the

**WHITMAN-WALKER CLINIC
WASHINGTON, DC**

and

AIDS ACTION COUNCIL

March 23, 1989

*submitted by:
Dr. Peter Hawley*

Thank you Mr. Chairman.

My name is Peter Hawley. I am a physician and a board certified pathologist. Currently I serve as the Medical Director and the Laboratory Director of the Whitman-Walker Clinic. Whitman-Walker is the largest AIDS service organization of the Washington D. C. metropolitan area. Before working at Whitman-Walker, I served for nine years as Director of Microbiology and Immunology at the Washington, D. C. Veterans Administration Medical Center.

I am here today to address concerns about so called "home testing" for antibodies to the Human Immunodeficiency Virus (HIV). I will speak both as a pathologist who has many years experience running immunology tests as well as the Medical Director of a community-based organization which has done HIV antibody testing since the FDA licensed the ELISA in 1985. I am also representing the interests of the AIDS Action Council, the national policy arm of AIDS service organizations around the country.

I will address standard testing protocols, the counseling and educational needs of those who seek the HIV test as well as describe the resources which community-based organizations can offer. I will also attempt to show why these needs cannot be met through most home testing schemes.

Like many other community-based organizations across the country, Whitman-Walker provides anonymous HIV testing. In 1988 we tested 4227 people for antibodies to the HIV virus. People who want to take advantage of our anonymous testing program make an appointment by giving us a code number. The client then comes in and receives pre-test counseling which takes about 45 minutes and includes information on the meaning of the HIV antibody test for both negative and positive results. We also offer HIV risk reduction counseling including information on safer sexual practices, condom use, and information on the proper use of needles. Clients are provided ample opportunity to ask questions about HIV transmission and are encouraged to do so. The ELISA and the Western Blot confirmatory tests are fully explained so that the client can understand the tests that are going to be done. After blood is drawn, the client returns in a few days for results. These services are provided, by the way, without cost to the client.

Our experience demonstrates that the time period between drawing the blood and receiving the test results is a very stressful one for many people. In fact, during the past two years we have known of at least four suicide attempts. When people return for results, these are given on a one-on-one basis with a trained counselor. Counselors go through an extended training program during which they learn to recognize serious emotional reactions. Reactions have varied from very mild stress to very severe psychotic episodes. On at least two occasions, clients have been hospitalized directly after hearing their antibody test results in order to prevent them from committing suicide. In order to meet this considerable support need, Whitman-Walker Clinic employs three counselors in this program and has a volunteer group of 75 counselors.

We have learned over the past several years that the routine counseling that occurs during the testing process is adequate for many people, but certainly not all. Many will go on to require further counseling in order to adapt to the knowledge of the positive test or to learn and sustain behavior changes whether or not they are positive. Like many other community-based organizations across the country, Whitman-Walker has developed a variety of individual and group support mechanisms for people who have had positive HIV antibody tests. Group sessions are scheduled on a drop-in basis. Usually these meetings attract about 15 people, many of whom have just heard of a positive antibody test result. People may attend these sessions for several weeks in order to talk with others who are experiencing the same problems. In addition, we provide individual drop-in times for those who wish to speak with a counselor on a one-to-one basis. Whitman-Walker also runs a variety of support groups for HIV positive people, many of whom are presently without significant symptoms of AIDS or ARC. These groups run for 15 weeks and average about ten people

per group. Presently, at least two of these support groups are exclusively for women. All of our HIV-positive clients are offered a referral into our HIV Medical Clinic, which can provide them with an evaluation for the presence or absence of signs and symptoms of HIV disease. Counseling relating to medical issues is given as an integral part of this service.

In spite of these various counseling opportunities, some people require much more intensive interventions. Thus the clinic recently added to its staff two full-time counselors who, at the present time, give 40 to 50 private counseling sessions per month to those people who are having trouble adjusting to an HIV positive result. Although these counseling experiences may last for as long as eight separate hour long sessions, many still require ongoing support. These individuals are referred to a network of psychologists and psychiatrists who have been identified by Whitman-Walker as being both sensitive and knowledgeable about HIV-related problems.

We have been repeatedly reminded of the devastating effects of antibody testing on peoples lives. Many equate a positive test result with a death sentence. Hours of counseling may be required in order to convince healthy persons that they, in fact, are in no immediate danger of dying. We estimate that of our average of 50 new HIV positive clients per month, 75 percent return to Whitman-Walker for medical evaluation and counseling. Approximately 50% require counseling beyond the initial post-test session.

Some will tell you that telephone counseling is adequate when disclosing test results. If this is true, then why do so many people who have access to face-to-face counseling need to be referred on for far more intensive support? How will these private companies, be able to adequately assess an individual's level of stress and counsel and refer for ongoing support?

Those who would provide for-profit home testing will tell you that home testing is needed because relatively few people return for their test results. At Whitman-Walker, 90 percent of those individuals tested for HIV have returned for their test results. We anticipate that as results become available faster (even now it is usually less than one week between the time when blood is drawn and results are ready), even a higher percentage will return. In addition, those who would advocate home antibody testing will tell you this is necessary because many people are not willing to go to a "gay clinic" in order to be tested. Community-based organizations across the country, including those founded by the gay community, have developed a knowledge and expertise in AIDS which is respected throughout their communities. Their services are well utilized by many different communities. In 1988, Whitman-Walker provided anonymous HIV antibody testing to a population that included 40 percent heterosexuals. With a variety of testing opportunities available, both within public and private clinics as well as in private doctors' offices, there seems to be little to suggest a need for home testing which has such a limited possibility of providing the necessary counseling support.

Confidentiality in HIV testing cannot be over stressed. Many come to anonymous testing sites such as Whitman-Walker precisely because their anonymity is guaranteed. Most of our clients can well afford a visit to their private doctor, but fear having the results of their test appear in medical records or reported to governmental authorities. In fact, many choose anonymous testing sites over any other facility for exactly this reason. Proposals for home testing bring up serious questions of confidentiality. Most schemes necessitate knowing the clients name, address or telephone number in order for test results to be returned. If that information is attached to the test results, clearly there is no anonymity.

Several techniques to get the tests results back to the client have been proposed, including telephone calls and letters. Notification of test results through the mail does not allow for the educational and behavioral modifying experiences and makes any supportive counseling impossible. Giving results by telephone would, at best, be only marginally better. Much of the information which the counselor uses to assess stress in the patient is visually acquired. In some clients, the only evidence of a serious reaction is a wringing of the hands or a twitching of facial muscles, while the voice may not communicate the severe anxiety that

the patient is experiencing. People who have done crisis and suicide telephone counseling can tell you of the sense of helplessness and sadness they feel when a suicidal person disconnects.

I would like to change pace at this point and now address you in my role as a pathologist and laboratorian. I have very serious concerns about blood collection by anyone other than a trained phlebotomist. A sample which has been poorly handled, either within the home or during transportation, can easily become inappropriate for testing. Increased levels of both false positive and false negatives results should be expected. Using temperature as an example, the proteins which make up the antibodies in the blood are denatured or destroyed by high temperatures and can also be inactivated by repeated freezing and thawing. It is not inconceivable that these kinds of fluctuating conditions could occur during transit through the mails. If the test results are any less accurate than the presently available test results, the consequences could be disastrous.

To give you some examples, let me tell you of three different people who came to our attention after having inaccurate testing or inadequate counseling by others. These individuals are people who came to us for confirmation of a positive test result they had received. The first was a young woman who had been told that she had a positive test and who, over a period of 6 months, made two suicide attempts. When finally coming to us for testing -- she was found to be negative for antibodies to HIV -- she was an emotional cripple. A second woman, when told of a positive test at the beginning of her pregnancy, decided to check with us before going ahead with a planned abortion. Luckily, she was also found to be HIV antibody negative. A third example was a young man who, in fact, had originally had a negative test. His physician had improperly interpreted that result and told the patient that he was a high negative and could be a borderline positive. When we had retested the patient and found him to be quite convincingly negative, he had already told his parents that he was dying of AIDS and had quit college. Even in the best of systems rare mistakes can happen, but it is important that we do not create more difficulties by expanding the possibilities for sample error.

Please don't construe anything I have said to suggest that I am against HIV antibody testing. Quite the contrary! I am director of a program which last year tested well over 4000 people and will likely test even more this year. In addition, I thoroughly believe that, with proper education, people do learn to make significant changes in their behavior: to decrease their risks of HIV infection or decrease the potential of infecting others. But HIV testing without accurate, sensitive and knowledgeable counseling and without absolute confidentiality guarantees is dangerous. We, as a society, need to make HIV testing and counseling more readily available to all who seek it, particularly those who are at any risk of being infected with the HIV virus. Unfortunately, home testing will not acceptably solve this problem but only provides a profit for those who would capitalize on the pain and fear of HIV infection.

Thank you.

Association of State and Territorial
Public Health Lab Directors

Written Testimony on Mobile Medical Laboratories
and Laboratory Home Test Kits

Presented before the United States House of Representatives
Committee on Small Business
Subcommittee on Regulation and
Business Opportunities

Mr. Chairman and members of the Committee, my name is J. Mehsen Joseph, Ph.D., Director of Community Health Surveillance and Laboratories Administration, Maryland State Department of Health and Mental Hygiene. I appear before you today as President of the Association of State and Territorial Public Health Laboratory Directors to present the position of the Association on the issues of home test kits and mobile laboratories/shopping mall and store front testing.

The Association has great concerns about the possible relaxation of the Food and Drug Administration's position on approval of home test kits designed for the diagnosis of infectious and communicable diseases. Over the past few years the Food and Drug Administration has approved several laboratory test kits for home use for non-infectious diseases. However, more recently a number of research institutions and manufacturers have succeeded in developing rapid tests for the diagnosis of various infectious and communicable diseases. Examples of such tests are those used to detect Group A Beta hemolytic Streptococci in children with septic sore throat, to detect Neisseria gonorrhea and chlamydia in sexually transmitted disease, and to diagnose urinary tract infection. Recently the FDA also licensed a rapid slide latex agglutination test for the detection of human immunodeficiency virus antibody in the blood of individuals. It is only a matter of time before commercial organizations attempt to convince the FDA that approval of these diagnostic kits as home test kits serves a public need.

We have strong reservations regarding the approval of such diagnostic home test kits. Diagnosis and management of an infectious disease requires a comprehensive approach in order to rule out non-infectious causes (e.g., cancer, etc.) and clinical acumen to override test results that do not conform to clinical judgement. It has been stated that when a physician makes a diagnosis of disease, 70 percent is based on the medical history, 20 percent on the physical examination, and 10 percent on laboratory tests. The

information obtained by Medical history and physical examination determines which lab tests the physician would request. For home test diagnostic kits, the procedure is reversed and ignores 90 percent of the diagnostic process. Placing kits in the hands of consumers will render a vast group of individuals unavailable for such physician scrutiny.

Home testing by consumers should be limited to on-going monitoring activities under the supervision of a physician. Thus, glucose monitoring has proven to be a useful system but it could well be managed by distribution of such kits by prescription. This would insure that individuals received training by their physician in the use and interpretation of tests.

Recent data (N. Engl. J. Med. 320:320-321, 1989) suggest that home use test for pregnancy fail at a substantial rate when performed by lay persons. False negative results promote activities that are inconsistent with good prenatal care, including smoking, drinking. False positive results must surely generate social problems that are not inconsiderable.

The Association of State and Territorial Public Health Laboratory Directors opposes the approval of any type of home test kit for the self-diagnosis of infectious or communicable diseases for the following reasons:

1. Use of home test kits for self-diagnosis of communicable diseases may lead to inadequate and/or inappropriate self-treatment. This self-treatment could lead to the development of drug resistant strains of various human pathogenic microorganisms spreading through the community without the knowledge or awareness of public health authorities. Such drug resistant disease producing agents could thwart the prevention efforts of public health officials.
2. Use of home test kits would bypass mandatory reporting requirements of evidence of communicable diseases to public health authorities and could impede public health control measures designed to prevent the spread of communicable diseases in the community.
3. A person using a home test kit to detect an infectious disease agent must be capable of performing the test with proficiency the first time it is attempted. Clearly, it is rarely ever possible to be proficient the first time one performs a new test procedure. In most instances home test kits will cost as much or more than conventional tests performed in an approved clinical microbiology laboratory.

4. Lack of skill on the part of the lay person coupled with inappropriate or incorrect use of the test may lead to incorrect interpretation of test results. This deficiency could give the person an unjustified sense of security or it could cause the person to over react to a positive test result.
5. Elimination of pre- and post-test counseling and the interpretation of test results by a qualified health care provider in the case of a positive test for HIV antibody could cause the person to adopt life-threatening or self-destructive behavior. Approval of such tests for home use could lead to tragedies associated with incorrect interpretation of test results and/or false positive test results and the lack of appropriate counseling by health care professionals. A false negative test result could give the person a false sense of security and lead to further spread of the disease in the community.
6. If a person is symptomatic, he should seek medical care from a qualified health professional rather than attempt to utilize a home test for self-diagnosis.

Regardless of the results of a home test kit, a person with symptoms should be seen by a physician at which time the test usually would be repeated in a laboratory if the clinical impression would so indicate. Nothing is gained by a patient attempting to self-diagnose his illness by using a home test kit.

I would like to specifically address the Association's concern about the potential licensure of home test kits and blood collection kits for detecting infection by the AIDS virus.

The Association strongly believes it would be a great disservice to the public health to allow the licensure of a home test kit for testing for infection to HIV (AIDS virus). It is a test which is not simple to perform and requires an experienced person to properly interpret the results. Even in the hands of a trained laboratorian performing the test in a licensed medical laboratory, it requires about one week of test use to be able to read the test reliably. It is unreasonable to expect a lay person to take a home test kit and perform the test accurately the first time. Also, studies by trained laboratorians reveal that false positive and false negative test results occur not infrequently. Therefore, no screening test for HIV has any validity until it has been subjected to the more complex confirmatory tests performed in an approved or licensed laboratory.

A false negative result in an HIV antibody test would convey a false sense of not being infected when in fact the person

may be harboring the AIDS virus and spreading it unwittingly. A false positive test could result in serious emotional/psychological problems that might lead the individual to self-destructing behavior.

HIV testing without appropriate counseling and education serves no useful public health purpose. Home testing for HIV could greatly compromise the opportunity for health professionals to offer testing in conjunction with counseling and education which would provide the maximum public health benefit from such testing.

Neither blood collection kits for home use nor home test kits for HIV antibody testing serves a public health need. In fact, they would hamper current programs initiated by state and local health departments across the United States to provide free counseling and testing, high risk behavior modification, partner notification, and other public health measures which might be helpful to contain the spread of infection. Surely the quality of service will deteriorate and the delivery of health care will be impeded by the widespread use of home test kits for HIV antibody.

I want to restate that the Association of State and Territorial Public Health Laboratory Directors opposes approval of any type of home test kit for the diagnosis of communicable or infectious diseases. The use of such home test kits would not significantly reduce the cost of health care or improve health care and could lead to a number of adverse reactions including possible crises or life-threatening situations. Significant harm to the individual, as well as to the community, could result from the spread of infectious agents and from the spread of drug resistant communicable disease agents.

I would now like to discuss the Association's concern about the mobile laboratory test unit and shopping mall/store front laboratory testing. The American public is developing a strong interest and a certain sophistication in matters of personal health. This interest has been stimulated by the profusion of reports of health studies in the news media and by the efforts of public interest groups and manufacturers of portable instruments and test kits. As a consequence of these promotional efforts, screening programs for cholesterol, diabetes, as well as chemistry and hematology profiles in unregulated mobile test units, shopping malls and storefronts are proliferating throughout the nation. Screening on a limited basis has long been performed at health fairs sponsored by civic groups and health-oriented groups, usually at no cost to the individual. However, massive screening is now taking place in mobile test units, shopping malls, storefront test sites, and even in supermarkets, usually for profit. Such screening as a preventive health measure can be a valuable educational tool

in motivating the public to adopt lifestyles which contribute to better health. But such screening should never be considered a substitute for the patient with symptoms or conditions requiring the personal attention of a physician.

Reliable results with this type of screening, as with all clinical testing, can only be obtained when the individual performing the test is adequately trained in the performance of the test and in the established principles of good laboratory practice, quality control, quality assurance, and equipment maintenance.

The Association of State and Territorial Public Health Laboratory Directors supports screening as a preventive health measure, provided certain precautions are adopted to safeguard the public from individuals inadequately trained and instruments improperly maintained. The Association is concerned that such safety measures are not now uniformly applied throughout the nation. Accordingly, the Association urgently recommends that the following guidelines be imposed on all such testing:

1. Testing should be performed only by adequately trained personnel. Training should be conducted by an individual with extensive knowledge and experience with the instrument. Training should include the principles of testing, the precise manner in which to perform the test, and understanding of quality control and quality assurance, calibration of the instrument, limitations of the test procedure and proper maintenance of the instrument.
2. The screening program should be conducted under the direction of a qualified laboratory person. In addition, an individual who qualifies at the level of a medical technologist should be on the premises at all times testing is performed. The supervisor should be qualified to provide the training necessary to perform the test, including instrument calibration and maintenance, to insure that reliable results are being generated.
3. An instrument used for screening should be approved by the same quality assurance testing as any other new laboratory instrument before being used on-site. It should meet established criteria with documented precision and accuracy. The procedure used on-site should follow the quality assurance/quality control standards required of laboratory testing procedures performed in the traditional laboratory.
4. Laboratory testing performed in mobile test units, shopping malls or storefronts should have the approval

of the appropriate health authority. This approval is to assure that the health authority (1) is aware of and endorses the screening activity, (2) will monitor and assure that the criteria herein outlined are met, and (3) can coordinate such screening efforts to assure that the community is best served.

5. The sponsor or testing group should provide educational material about the specific test and the specific condition. Such material should state the test limitations, normal ranges, and what to do if the results are outside the normal limits. The material should include information about the condition or disease, relative risks, and its symptoms. The material should be brief, succinct, without excessive medical jargon, and in large print. The sponsor or testing group should be responsible for having a physician or other qualified health professional available on-site to answer questions that might arise regarding test results. To insure proper follow-up, the individual in charge of the screening program should contact all patients with abnormal results within a reasonable period of time to emphasize the need for the person to see a physician.
6. The sponsor or testing group should have liability insurance to cover the screening program. This would minimize the likelihood of unscrupulous or unethical practices. Most consent forms utilized contain disclaimer statements; however, the sponsor or testing group should be held accountable for any injury incurred as a result of negligence in testing including the dissemination of inadequate or inaccurate information.

In summary the performance of medical laboratory testing in unconventional sites such as mobile test units, shopping malls and storefronts raises great concern about the quality and medical usefulness of this kind of testing because it is usually performed by poorly trained individuals who lack the appropriate knowledge and experience. Mobile laboratory test units are unregulated in most states. Only a few states (MD, PA, FL) have banned this kind of testing which usually occurs in shopping malls, storefronts, and worksites.

Individuals performing lab tests at these unconventional sites generally are non-laboratory trained and lack knowledge about quality control/quality assurance practices essential to providing reliable lab results. An example is fingerstick cholesterol screening made possible with the development of portable instruments purported by the manufacture to be simple to operate. Studies have shown that under the best of conditions in shopping mall testing or mobile labs about 25 percent of the people tested are

misclassified as to their risk while under less stringent conditions approximately 50 percent of those submitting to cholesterol testing are misclassified. The result is that some individuals whose values are reported as falsely low values fail to seek medical attention while those with falsely high values are referred unnecessarily for costly medical follow-up. Even in the regulated medical lab where strict standards of quality control/quality assurance measures are performed each day testing is performed, there can be significant variability in cholesterol test results. It is unreasonable to expect that testing in unconventional sites which are unregulated could be expected to perform at an acceptable level of quality. Finally, several issues arise in regard to mobile laboratory test units and shopping mall/storefront testing: 1) Who is authorized by state law to penetrate the human body to collect a specimen?; 2) Who is permitted by state law to request a lab test?; 3) Who is permitted by state law to receive test results?; 4) Are the infectious waste laws/regulations being complied with at these sites? Although these issues are not clearly defined in some states, the HCFA regulations for independent labs restrict requests for tests to health professionals who are authorized by state law to request medical laboratory tests. Release of lab report data is to the physician or submitter.

Mr. Chairman I thank you for the opportunity to present the concerns of the Association about unregulated mobile test units and laboratory home test kits and also to proffer our recommendations.



AMERICAN PUBLIC HEALTH ASSOCIATION

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WILLIAM H. McBEATH, M.D., M.P.H., *Executive Director*

February 13, 1989

Dockets Management Branch (HFA-305)
Docket No. 87D-0119
Food & Drug Administration
Rm 4-62
5600 Fishers Lane
Rockville, MD 20857

Re: Assessing the Safety and Effectiveness of Home-Use In Vitro Diagnostic Devices (IVD's): Draft Points to Consider Regarding Labeling and Premarket Submissions

The American Public Health Association has reviewed the concept of Over-the Counter (OTC) test kits for infectious diseases. The Association has strong reservations regarding the approval and introduction of such kits. Diagnosis and management of an infectious disease requires a comprehensive approach in order to rule out non-infectious causes (e.g., cancer, etc.) and clinical acumen to override test results that do not conform to clinical judgement. Placing kits in the hands of consumers will render a vast group of individuals unavailable for such physician scrutiny.

Home testing by consumers should be limited to on-going monitoring activities under the supervision of a physician. Thus, glucose monitoring has proven to be a useful system but it could well be managed by distribution of such kits by prescription. This would insure that individuals received training by their physician in the use and interpretation of tests.

Recent data (N. Engl. J. Med. 320:320-321, 1989) suggest that home use test for pregnancy fail at a substantial rate when performed by lay persons. False negative results promote activities that are inconsistent with good prenatal care, including smoking, drinking. False positive results must surely generate social problems that are not inconsiderable.

Should the FDA decide to expand home testing by consumers into the infectious disease arena, the Association would strongly advise the introduction of new rules for adoption and continued acceptance of such kits. Kits currently FDA approved for in-vitro microbiologic diagnosis by

professionals are prone to failure at a fairly high rate. Laboratorians, however, can often detect these failures by 1) trends in high positive or high negative rates, 2) concurrent testing with other test modalities, and 3) clinical acumen and complaint. Thus, failing kits are discarded or the results disregarded. When placed into use in the home, similar safeguards will be unavailable to the users. Thus, APHA strongly recommends that home test kits be performance monitored by an independent laboratory throughout their marketed life. The draft document addresses the approval mechanism for home test kits without introducing on-going monitoring. Thus, it is not acceptable to the APHA.

There are a number of other major areas where the draft document requires considerable revision to clarify and specify requirements to the manufactures.

1. User Demographics

Preapproval evaluation of test kit performance by consumers should clearly delineate the demographics of the individuals who used the test. A low income group composed mainly of graduate students in a university town does not constitute a true low income group. Furthermore, evaluating the kits in a shopping center generally excludes those individuals who shop in inner cities and do not have transposition to shopping centers. Education (grades completed) would clarify this to some extent. If bilingual instructions are to be made available, users should test the kits using the instructions that they are able to read and data should be kept relative to the performance of the translated instructions.

If the results of preapproval evaluations suggest that the kit usage should be limited to certain demographic groups, then the package should clearly state those limitations.

2. Package Labelling

The package insert should clearly specify the sensitivity and specificity of the kit's performance, as done by lay persons, when compared to the reference method done by professionals. The term specificity and sensitivity should not be used, however, nor should percentages. For example, one could say that the test detects 9 out of 10 individuals with strep throat, thus 1 in 10 will be missed. Furthermore, the advertising and package labels should not be allowed to project a value judgement relative to the performance parameter. For example, the test which detects 90% of all positives cannot be billed as "accurate".

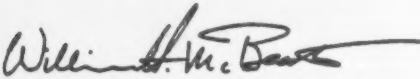
The manufacturer should be required to maintain a toll-free number and an address where users might call or write. The toll-free number should be available for inquiry Monday

through Friday 8 am eastern time to 5 pm pacific time, the package insert should also specify a number for users to call at the FDA when the manufacturer does not comply with these requirements. Finally, users should be advised not to call their local laboratories, since laboratorians will not be familiar with the specific test in question. —

APHA has a particular objection to the use of home testing for the presence of HIV antibodies. At the present time the only way to break the chain of transmission of HIV infection is to foster behavioral changes through education. For this reason APHA strongly believes that the test for the presence of HIV antibodies must always be accompanied by informed consent along with pre- and post test counseling about the meaning of the test, the nature of HIV transmission, and the prevention of HIV infection. The opportunity to provide counseling the education will be lost if home test kits are made available. In addition, there is a potential for discrimination due to the involuntary use of the test by employers and insurers.

In summary, the draft document requires considerable revision, should the FDA decide to approve home test kits for infectious diseases. FDA approval of test kits will inherently suggest their acceptable performance. Preferably, however, the FDA would decide to introduce new rules regarding the monitoring and regulation of such kits, as addressed above. Further we urge the Agency to consider carefully the impact home tests kits will have on public health effects to prevent the transmission of communicable diseases.

Very truly yours,



William H. McBeath, MD, MPH
Executive Director

TESTIMONY OF VINCENT R. VALLES, SR., PRESIDENT,
INTERNATIONAL MEDICAL TECHNOLOGIES, INC. [IMT]

Testimony before the United States House
of Representatives, Subcommittee
on Regulation, Business and Energy

Subject: AIDS/HIV Virus Testing

IMT MEDICAL CENTERS
HIV TESTING FACILITY

IMT Medical Centers were established as a result of 18 months of research by the parent company International Medical Technologies. Research was conducted on the medical use of Tri-Atomic Oxygen (Ozone). Our initial interest centered on the European use of Tri-Atomic Oxygen in the treatment of AIDS patients. The company conducted a worldwide search on the medical use of Ozone. (List of available abstracts attached) Research indicated that Tri-Atomic Oxygen had been used successfully since 1912 in Europe to treat various viruses. Recent abstracts indicate successful treatment of the AIDS virus using this modality.

Based on the encouraging results of our research, we contracted the services of Hazleton Laboratories. They prepared a preliminary regulatory strategy for the development of our TAO generator for the purification of blood and blood products. In Hazleton's opinion the most prompt route to the market was to develop the products use in the treatment of blood. Treatment of AIDS was a much longer involved process. In order to fund the ongoing research, the Company determined that a viable means of obtaining the necessary capital resources had to be established.

It became apparent to the management of the Company that an opportunity existed in providing facilities to test for the HIV virus in a confidential setting. It appears the emphasis both medically and politically is on those individuals who have progressed to full-blown AIDS. There are indications that early detection of the virus and consultation regarding behavior, nutrition and attitude changes should be the focus of our attention. We have surveyed HIV positive individuals, individuals in the ARC stage, AIDS patients and local and national support groups. The surveys produced the following information:

1. HIV positive individual fell into three groups:
 - a. Waiting to Die
 - b. Continuing their existing life style
(with total disregard for others)
 - c. Under the care of a Physician
2. ARC patients:
 - a. Extremely well informed and searching an answer
 - b. Seeking alternate treatment modalities
3. AIDS patients:
 - a. Subscribing to traditional treatment primarily AZT
 - b. Seeking alternative unapproved treatments
 - c. Seeking treatments in foreign countries

CUSTOMER MARKET

It was determined by management that our services should focus on those individuals who are at risk, who proved to be HIV positive and who are in the early stages of ARC. The following represents the at risk groups:

1. Single individuals with multiple partners
2. Individuals considering marriage or entering into a long term relationship wanting to be assured that they were not jeopardizing the other party
3. Individuals in the high risk groups who concluded they needed to know
4. Individuals concerned as a result of a blood transfusion
5. Individuals working in medical facilities

CAMBRIDGE BIO-SCIENCE

We first became aware of the "Quick Test" in an article in the November issue of U.S. News and World Report. The Pandex Division of Becton Healthcare Corporation, the marketing company for the "Quick Test", responded to our inquiry. They were cautious in allowing us access to their product. Pandex personnel were extremely helpful in instructing us on the proper use and in evaluating the results. Our protocol is as follows:

1. The attending physician conducts pre-test counseling
2. A Registered Nurse trained in this testing process administers the test.
3. If the test proves positive a second test is performed. If both test are positive the patient is informed that the test is inconclusive and a Western Blot test is performed by an outside lab. (The patient is not charged for the second test or the Western Blot)
4. The attending physician conducts post-test counseling

We believe that being able to provide a quick screening test is important to the public. Patients testing negative for antibodies to HIV express relief and appreciation for not having to wait up to two weeks for the results. We believe that the "Quick-Test" has been instrumental in encouraging people to be voluntarily tested.

STATE AND FEDERAL REGULATIONS

As we have just opened our Business we have not experinced any difficulties on a State or Federal level.

It is my opinion that Americans do not yet understand the consequences of the HIV epidemic. It has begun to enter the general population. This will bring it close to every household in America. This IS happening and we MUST address the following issues.

1. We MUST develop medical capabilities and facilities to meet this problem
2. We MUST provide private and public funding to address the added case load.
3. We MUST develop facilities to test the estimated 40 million people needing to be tested NOW.

Whenever conditions such as these face a nation it brings out the best and the worst in Americans. We believe that it is imperative that proper training and regulations be enacted. These are required to ensure that the American people receive the very best testing, treatment and counseling in the fight against HIV (AIDS). It becomes more apparent that we need to devote as much energy and resources to the source (HIV) as to the results (AIDS) of the problem.

MEDICAL ABSTRACTS

Our research on the use of Tri-Atomic Oxygen for medical applications has resulted in our obtaining several abstracts world wide. Some of which are pertinent to our project and are available upon request.

1. TITLE: The Preussch AIDS-Therapy
AUTHOR: Alexander Preussch
COUNTRY: West Germany
2. TITLE: Ozone Inactivates Extracellular Human Immuno-
deficiency Virus at Non-Cytotoxic Concentrations
AUTHOR: Dr. Michael T. Carpendale & Joel K. Freeberg, M.A.
COUNTRY: Sweden
3. TITLE: The Biochemical Processes Underlying Ozone Therapy
AUTHOR: R. Viebahn & Dr. J. Mansler
COUNTRY: West Germany
4. TITLE: The Clinical Effects and Biochemistry of Ozone
Therapy in Peripheral Arterial Circulatory
Disturbances
AUTHOR: Otto Kar Rokitansky
COUNTRY: Austria
5. TITLE: The Basic Clinical Applications of Ozone Therapy
AUTHOR: Dr. Siegfried Hilling
COUNTRY: West Germany
6. TITLE: Ozone and Biological Species
AUTHOR: Dr. John H. Walton
COUNTRY: U.S.A.
7. TITLE: Ozone vs. Hepatitis and Herpes - The Choice
AUTHOR: Dr. Heinz Konrad
COUNTRY: Brazil
8. TITLE: The Treatment of Viral Hepatitis with Ozone-Oxygen
Gas Mixtures
AUTHOR: Dr. Hartmut Dorstewitz
COUNTRY: West Germany
9. TITLE: Ozone as Therapy in Herpes Simplex and Herpes Zoster
Diseases
AUTHOR: Dr. M. Mattassi, Dr. F. D'Angelo, Dr. A. Franchina,
Dr. P. Bassi
COUNTRY: Italy
10. TITLE: Study of Chronic Hepatitis and Ozone Therapy
AUTHOR: Prof. Horst Kief, M.D.
COUNTRY: West Germany
11. TITLE: Ozone Application in Cancer Cases
AUTHOR: Dr. Joachim Varre
COUNTRY: West Germany
12. TITLE: Experiences of a Pediatrician using Ozone as a
Chemotherapeutic Agent for the Treatment of Diseases
of Children
AUTHOR: Dr. Robert A. Mayer -- Co-Founder of I.M.T.
COUNTRY: U.S.A.
13. TITLE: Use of Ozone as a Chemotherapeutic Agent for the
Treatment of Acute Monocytic Leukemia and Adeno-
Carcinoma in Mice
AUTHOR: Dr. Robert A. Mayer
COUNTRY: U.S.A.
14. TITLE: Ozone in the Dental Practice
AUTHOR: Dr. Fritz Kramer
COUNTRY: West Germany

Testimony of Elliott J. Millenson

United States House of Representatives
Committee on Small Business

The Subcommittee on Regulation, Business Opportunities and Energy

March 23, 1989

Mr. Chairman. Based on my experience as founder and chairman of a company which developed and tested in clinical trials an AIDS home-test, I can say that the concept of AIDS home-testing makes sense, it is feasible to implement and the potential benefits appear to be far greater than potential risks.

INTRODUCTION

The AIDS home-test my company developed and tested was a home blood collection kit. This means that people would use the test kit to collect a blood specimen onto special paper, and then send that specimen by pre-paid mailer to our laboratory for testing. All specimens would be tested by screening and confirmatory methods.

Pre-test counseling would be provided via educational material included in the kit and through access to a toll-free hotline. Results, counseling and education would be received anonymously over the phone from trained health care professionals.

In December, 1987, after completing clinical trials and other research we submitted an application for marketing approval to the FDA. In March, 1988 the FDA announced a policy, based on input from advisory groups and interested parties, that no AIDS home-tests would be allowed, regardless of their accuracy. Because of this policy, the FDA has continued to decline to study research data from any company demonstrating the safety and effectiveness of AIDS home-tests.

While it is unprecedented for a company to disclose research data prior to product approval, since the FDA will not study our data, I will discuss our findings this morning to help shed light on the issue of AIDS home-testing and to increase awareness that the only difference between AIDS home-tests and current AIDS tests is that the specimen is collected in the home.

CONCERNS

I have been asked to address specific concerns which have been raised about AIDS home-tests.

1) Can Laypeople Collect an Adequate Blood Specimen?

Yes.

Experience with home blood glucose test kits has already shown that lay people are capable of doing a fingerstick and obtaining an adequate amount of blood for testing without special training. Additionally, we confirmed that people could collect an adequate blood specimen in clinical trials with a large number of volunteers from all socioeconomic groups.

2) Is there a Safety Risk When Collecting a Blood Specimen in the Home?

No.

In clinical trials, there were no user safety problems. This is consistent with research data on the use of home glucose monitoring tests.

Additionally, we found use of the test kit posed no safety problems to others. Public health officials agree that there is no significant risk of infection from potentially HIV contaminated blood which we encounter in our everyday lives, such as blood from razors, toothbrushes and sanitary napkins.

3) Can Blood Specimens be Shipped Safely?

Yes.

In our clinical trials, it was established that people could safely package and ship specimens for mailing. I should note that blood specimens -- even AIDS blood specimens -- are already routinely shipped by mail to laboratories around the country every day. Most of these specimens are in test tubes which could break or spill -- compared to my company's home test specimens which were dried spots of blood on a piece of paper.

My company's test kit included special packaging to withstand potential unusual and adverse shipping conditions. I should note that we selected Federal Express to ship our specimens, and that I met with their chairman to discuss our product. After thorough tests on our packaging, Federal Express agreed to carry our specimens having determined that our package posed no danger to their employees.

4) Are AIDS Home-Test Results Accurate?

Yes.

We found a 100% correlation between HIV antibody results obtained using our test kit and results obtained by a traditional venipuncture method, that is a doctor drawing blood from the arm.

This high degree of accuracy for the method we used has been confirmed in similar independent research done by the Johns Hopkins School of Public Health. The CDC has found the test method my company used to be so safe and reliable that they are currently using the identical method for a nationwide study to assess the presence of HIV antibodies in newborns.

We also determined that accuracy of test results were not affected by extremes in temperature or delays in shipment. These findings confirmed similar independent studies conducted at the Johns Hopkins School of Public Health.

5) Is it safe to provide Counseling and Education over the Telephone?

Yes.

Some critics of AIDS home-tests have expressed concern that giving people AIDS test results over the phone may lead to adverse consequences. They're right. And their concern is justified. But -- even with the finest face-to-face counseling -- there can be adverse consequences. After receiving test results sometimes people may knowingly or unknowingly infect others, become confused about the meaning of test results, or attempt suicide. The real question is this: Is providing test results over the phone less safe than providing results in a face-to-face setting?

Despite widespread concern, evidence suggests that there is no increased risk. Research by psychologists who are experts in the fields of telephone counseling, suicide prevention and AIDS counseling, suggest that there is a minimal difference in the effectiveness of counseling over the phone -- when it is done well -- compared to counseling received in face-to-face settings. The fact is -- people are already getting AIDS test results over the telephone. Doctors frequently use the telephone to provide patients with lab test results including results for AIDS and other fatal diseases such as cancer biopsy results.

Additionally, there is a popular misconception that everyone who gets tested for AIDS gets counseling. This is simply not true, as dramatically revealed in a recent study published in the *Journal of the American Medical Association*. While public health clinics always provide counseling, this study showed that 75% of people choose to get tested in other settings, and often do not receive counseling.

One final point on counseling: telephone counseling is already widely used

in centers specifically established for that purpose -- in information centers such as the CDC's AIDS Hotline -- and in crisis intervention centers such as suicide prevention and poison control. Professional counselors trained in telephone counseling, crisis intervention and AIDS counseling can effectively provide AIDS counseling and information over the telephone.

BENEFITS

And, there are potential benefits to making AIDS home-tests available.

1) Only Testing Can Provide Knowledge

According to CDC estimates, as many as 1.5 million Americans may be infected with the HIV virus. In a recent study conducted at University California San Francisco, the median time from HIV infection to onset of symptoms of AIDS was found to be 9.6 years. During that incubation period, a person shows no outward signs of HIV infection.

Yet, the majority of HIV infected people are unaware of their infection. So, for 10 years, there is a potential that they will unknowingly infect others, as well as fail to seek potentially life-prolonging medical treatment for themselves. And in this way infection continues to spread and spread again. Only testing can provide knowledge of HIV status so that people do not risk infecting others or becoming infected simply because they didn't get tested.

2) Home Testing Will Be Utilized

Several research studies have demonstrated that people who want to get tested for AIDS are reluctant to use current testing alternatives. The main reasons are fear that results will not be kept confidential or that testing will not be anonymous. Even some doctors recommend that their patients not get tested for AIDS, fearful that test results can't be kept confidential.

Some people are comfortable going to a doctor or a clinic for an AIDS test. But others are simply too embarrassed. Or they don't live near a testing center. Or they can't afford the test. Or they're just won't go to a VD Clinic to get tested because they're afraid that someone they know will see them.

CONCLUSION

The fact is that so-called "safe sex"-- the use of condoms -- is not considered safe when one partner is HIV infected. Studies have shown a high rate of infection even when condoms are used if one partner is infected. For this reason, the Public Health Service recommends "alternative forms of sex" not "safe sex" when one partner is known to be infected. We must use testing -- in conjunction with safe sex and education -- to help prevent the spread of AIDS -- and save lives. The

American Medical Association has recommended that "Tests for AIDS virus should be readily available to all who wish to be tested." But, many Americans won't use the testing alternatives which are currently available.

We are at a crossroads in dealing with the spread of a deadly virus. And we have taken the road less traveled. The road -- not of studying research and then reaching a conclusion -- but the road of reaching a conclusion without even examining the research. Robert Frost wrote of the road less traveled, "Yet knowing how way leads on to way, I doubted if I should ever come back." We must come back. Because that will make all the difference.

Thank you.

Elliott J. Millenson
Rockville, Md.

*Testimony of
Elliott J. Millenson
March 23, 1989*

EXTENDED REMARKS

Portions of actual sections, or quotes, from my company's PMA submitted to the FDA on December 30, 1987 are included as part of extended remarks.

INTRODUCTION

1) AIDS Home-Test Kit

An illustration of the interior components and exterior package of our AIDS Home-Test Kit is provided in this section. It should be noted that the name "AIDS CHECK" was used for research purposes only. In designing our test kit, we felt that the special requirements of AIDS testing necessitated a home blood collection kit, so that pre and post test counseling and education would be provided by medical personnel, and that highest level of test quality could be maintained. Such a test can combine the convenience and confidentiality of home testing, with the quality of a laboratory test and input of trained medical personnel.

As we stated in our PMA, clinical trials were conducted on:

"A large sample size (248 samples) was used in this study with a statistically significant representation of individuals from high, middle and low educational and socioeconomic levels."

2) FDA Response to AIDS Home--Tests

The FDA issued a statement responding to the illegal marketing of AIDS home-test kits by some companies in July, 1987. The FDA emphasized that AIDS home blood collection kits were, "medical devices which require premarket approval by FDA, a process which obliges the manufacturer to conduct clinical testing to show the test is safe and effective." In other words, manufacturers intending to market such kits would have to apply for premarket approval (FDA July 23, 1987 "Talk Paper titled, "Unapproved AIDS Home Test Kits). The FDA issued another "Talk Paper" on AIDS Test Kits on October 26, 1987, to indicate that "all activities within FDA related to diagnostic testing for AIDS are the responsibility of CBER [Center for Biologics Evaluation and Research].

On December 3-4, 1987, the Blood Products Advisory Committee of the FDA met in open hearings. The Advisory Committee discussed AIDS home-tests, and determined that guidelines for evaluating such tests needed to be established.

On December 30, 1987, my company submitted a premarket approval

application to the FDA.

On March 30, 1988, the FDA informed us that it was refusing to accept our application for a substantive review. In his March letter, Dr. Paul Parkman, director of the FDA's Center for Biologics Evaluation and Research, explained the agency's decision by stating that it sought "the advice and counsel of various advisory groups and interested parties." As a consequence of those discussions, the FDA had concluded that it would review applications only for those AIDS test products which met five criteria[note: these criteria are still in place and apply to any manufacturer who might want to submit a PMA]. The first two of those five criteria are:

"1) Kits must be labeled and marketed for professional use only within a comprehensive health care environment (e.g. hospitals, medical clinics, doctor's offices, STD clinics, alternative test sites, and mental health clinics).

2) Kits must provide for the collection of a venipuncture or other appropriately validated sample by one who is recognized by a state of local authority to perform such procedures."

The three additional criteria for an AIDS home-test can meet are:

"3) The testing sequence for all samples collected with the kits must include use of a licensed screening test for antibody to HIV and, for those samples testing positive an additional more specific test (i.e. Western Blot or comparable test). It is recommended that a licensed more specific test be utilized; however, the Agency may accept a properly validated unlicensed test until licensed tests are more widely available.

4) The instructions for sample collection, storage, shipping, and testing must conform with, or be validated as equivalent to, the package insert instructions for the specific licensed HIV antibody test kit used to test samples.

5) All results of testing must be reported directly to a professional health care provider for reporting and interpretation of the result to the requestor of the test, as well as for counseling of the individual."

Dr. Parkman closed his letter by stating:

"Although the criteria outline in items 1-5 above represent our current approach to the regulation of these devices, we plan to seek further public comment on such issues as lay person sample collection and shipping, and counseling outside of a medical setting."

A good perspective on my company's dealings with the FDA is found in an Op Ed article published in the *Wall Street Journal* on January 17, 1989 which is included with these remarks.

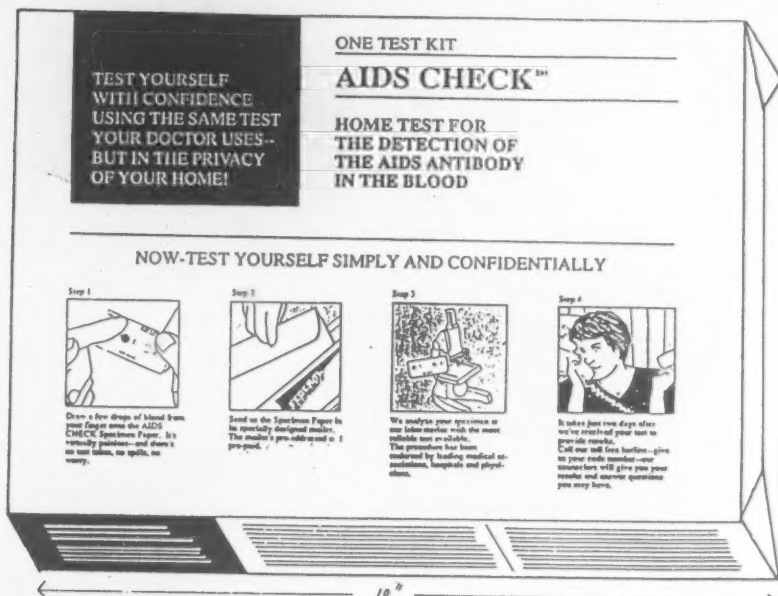
It should also be noted that my company did respond to the FDA's first two criteria (e.g. professional use only; comprehensive health care environment) by relabeling all outside packaging and revising package instructions. We felt this would at least be a way to get the application accepted and the data studied by the FDA.

My company submitted an amendment to our PMA to the FDA with these changes. The kit remained the same except that a physician would collect the blood sample in a health care setting. Results would be provided by telephone by my company's Counseling Center employees -- a center staffed by professional health care providers. The agency still refused to accept our application, noting in their October 12, 1988 letter:

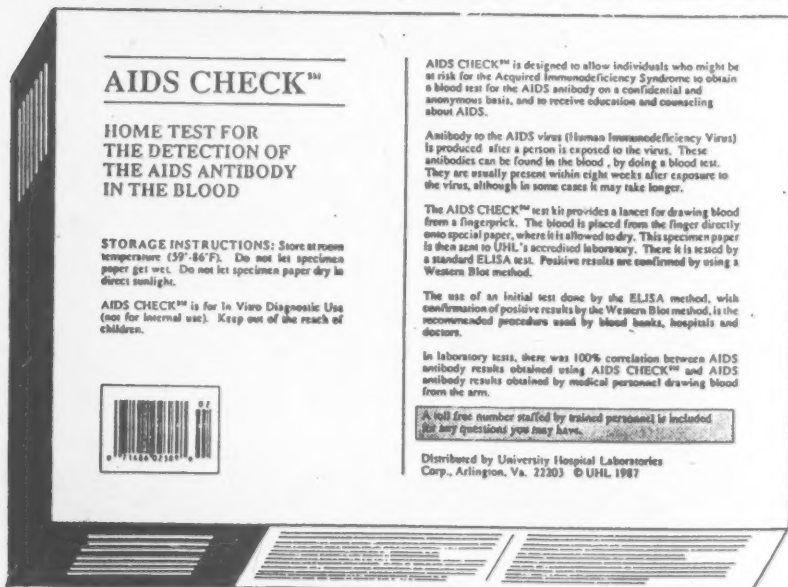
"Your revised labeling of the kit allows the person being tested to obtain test results directly from [your company]. Item #5 of our March 29 letter states that the test results be reported to a professional health care provider for reporting and interpretation of the results to the requestor of the test."

EXTERIOR VIEW OF AIDS CHECKSM

FRONT VIEW



BACK VIEW



THE WALL STREET JOURNAL.

TUESDAY, JANUARY 17, 1989

Why You Can't Take an AIDS Test in the Privacy of Home

By ELLIOTT J. MILLERSON

Two years ago, I formed Universal Hospital Laboratories to develop a home AIDS test. Although the company recently ceased operations, its failure was due not to problems with the product, but rather to lack of progress with the Food and Drug Administration.

In December 1987, after completing product development and testing, we submitted a marketing approval application to the FDA. We received several clinical health benefits of home testing, and detailed findings in such key areas as counseling and confirmation of positive results.

My company's home AIDS test differed from traditional home tests, such as home pregnancy tests, in that it allowed users to take a blood sample and then send the sample anonymously to our laboratory. Our company would test specimens using the identical method that doctors and hospitals use—the ELISA screening test and Western blot confirmation according to the protocol of the American Association of Blood Banks. The test user would obtain an 800 number and identify himself by the code number and name of the laboratory. Results, counseling and follow-up referrals would be provided over the telephone by our company's medical staff trained in AIDS counseling, crisis intervention and telephone counseling.

We did not feel that rapid screening methods, such as the recently FDA-approved Cambridge BioScience test, would be appropriate for home use, because we wanted to guarantee that all users received counseling and education, and that there would be the lowest possible level of false positives.

By statute, Congress has given the FDA 45 days to confirm that a marketing application is complete and acceptable for filing. Once the FDA has made that confirmation, it then has up to 180 days to complete the application on its merits.

Last March, 81 days after our application was submitted, the FDA informed us

that it was refusing to accept our application for filing and would not undertake the full substantive review. In his March letter, Paul Parkman, director of the FDA's Center for Biologics Evaluation and Research, explained the agency's decision by stating that it sought "the advice and counsel of various advisory groups and other interested parties."

At the time, the FDA had concluded that it would not review applications only for home AIDS test products that were "for professional use only within a comprehensive health care environment," and provided for the collection of the blood sample by "one who is recognized by a state or local authority to perform such procedures." Translation: an FDA review of any home AIDS test applications.

While the FDA would not review any such applications, the agency did say in March that it planned to "seek further public comment" so that it could develop a policy on home AIDS testing. In early September, responding to a July inquiry I made, FDA Commissioner John H. Hargis wrote me and indicated that the agency intended to hold a public meeting in the near future to provide an opportunity for all interested parties to express their views (which will be considered in the development of policy).

The FDA continues to maintain that hearings will be held soon, even as a study conducted in mid-1987 for University Hospital Laboratories concurrent with the clinical trials showed that more than 30% of respondents said that the only way they would get tested for AIDS would be via a home test like the one we developed, due to a desire for anonymity.

The FDA's unwillingness to study the evidence on home AIDS tests appears to be mostly due to pressure from AIDS activists and Congress. These groups oppose the sale of home test kits, arguing that even though it provides identical results to a test given in a medical environment, counseling it is impossible to provide AIDS counseling and support over the telephone.

not otherwise receive these services. The FDA should treat home AIDS tests like it treats any other proposed test—review the evidence from research studies and then reach a decision based on the scientific evidence presented. The FDA's "just say no" policy on the acceptance of applications establishes a guideline that is not only bad for the nation's public health but is a bad precedent for science as well. With it, the agency charges "with reviewing data before granting approval for the marketing of any new drug or medical test has indicated that it doesn't need to study new evidence before reaching a decision. Nothing is more likely to happen than the ability to market a drug or device before the agency has had time to adequately assess resources, risk and reward. Surveys demands the ability to rise dispassionately above the landscape, like a helicopter over a congested highway, and determine the best course. My company's course was set in the belief that the FDA would put safety before palliatives. We were wrong.

Our home AIDS test assured that education and counseling are always provided with test results—something that is not always the case with current AIDS tests. Some physicians receive results face-to-face while others receive results face-to-face with no explanation as to their meaning. The Journal of the American Medical Association reported in early 1988 on a study in which a significant number of patients did not receive counseling or an explanation of AIDS test results.

Many people are reluctant to get tested for AIDS because they fear test results will not be kept confidential. Embarrassment, waits of up to three months to be tested or mandatory pre-test group counseling at some clinics discourages others. As a result, they may be spreading the AIDS virus unknowingly. Patients are not alone in their fear. Some physicians will provide tests only when forms are signed releasing them from any liability if test results are revealed. But a home AIDS test using a coded identification number can be taken privately and anonymously, eliminating these objections.

Since December 1987, when we submitted our marketing approval application, more than 30,000 new cases of full-blown AIDS have been reported in the U.S. Recently the General Accounting Office studied the government's AIDS education efforts and criticized its "slow implementation of key activities." This prompted Barbara Boor (D, Calif.) head of the House Committee on Commerce, Science and Transportation to call for a "major effort to speed up the implementation of public education programs. Home AIDS tests could provide an alternative source of AIDS education and counseling—as well as testing—for the many people who might

Mr. Millerelson is a management consultant based in Rockville, Md.

*Testimony of
Elliott J. Millenson
March 23, 1989*

EXTENDED REMARKS

CONCERNS

1) Can Laypeople Collect an Adequate Blood Specimen?

For perspective, test kits to measure blood sugar level (blood glucose monitoring kits) are available over the counter and are successfully used by people with no special training. Regarding such kits, we concluded in our PMA:

"In fact, several studies have examined the ability of people without previous experience to perform home blood glucose monitoring. A review article in 1985 reviewed the literature on problems associated with the use of home glucose monitoring tests. Specific problem areas were identified. Difficulty in performing the fingerstick was not found to be a problem in adults..."

"Data on use of home glucose monitoring tests show that, although there are several areas of difficulty in test performance, adults do not exhibit difficulty in obtaining blood samples. This corroborates findings in clinical trials on AIDS CHECK."

Despite the research on glucose monitoring kits, we felt it was appropriate to conduct our own clinical studies to determine people's ability to safely collect an adequate blood specimen onto filter paper since collecting a specimen onto filter paper is slightly different than collecting a specimen for glucose monitoring.

It needs to be noted that clear, illustrated instructions was a key factor in people's ability to properly provide a blood specimen. Some people also called in to our "Counseling Center" for assistance. As we stated in our PMA:

"However, since the use of specific instructions and illustrations was found to be the single most important factor in determining whether people were able to correctly perform AIDS CHECK, the data on the ability of people to correctly follow blood drawing instructions in other manufacturer's products would not be expected to accurately reflect the ability of people to follow AIDS CHECK instructions."

2) Is there a Safety Risk When Collecting a Blood Specimen in the Home?

We were careful to select a lancet with superior safety related features to other marketed lancets to reduce risk of safety problems. We selected the lancet we used,

as we noted in our PMA, because it is:

"considered superior to other lancets currently marketed for home use because it has the following additional safety features:

1) *Automatic blade retraction* protects user from accidental stick before and after use.

The lancet blade is set within a protective plastic sheath before use. As soon as the blade has penetrated the skin and the plunger is released, the blade automatically retracts back into this protective sheath.

2) *Plastic safety guard* and unique blade design, designed for use in infants, assures safe depth penetration.

A plastic safety guard prevents the blade from penetrating more than the desired depth. A straight blade edge, instead of the pointed blade used in most lancets, assures safe and uniform depth penetration.

3) *Semiautomatic operation* allows ease of use and consistent penetration."

Our PMA additionally noted that:

"Several studies have examined the ability of people without previous experience to perform home glucose monitoring. A review article in 1985 reviewed the literature on problems associated with use of home glucose monitoring tests. Specific problem areas were identified. Difficulty performing fingerstick was not found to be a problem in adults."

Additionally, to reduce safety risks in the home we designed our test kit so that after taking a blood specimen, the user would place the specimen *and* the used lancet into the custom-designed plastic shipping container. The lancet fit into that container in much the same way a used single-edge razor blade fits into the back of a pack of razor blades. That is, once the lancet was placed in the container, it could not be removed. It would be disposed of at the laboratory.

We planned to develop single-unit blood collection device which encased a lancet and filter paper and allowed automatic collection of a specimen onto filter paper after a user placed the device on their finger and pressed a button to draw blood. Our medical advisors and packaging experts expressed confidence that such a design was feasible.

3) *Can Blood Specimens be Shipped Safely?*

It should be noted that Federal Express routinely ships AIDS blood specimens as does the U.S. Postal Service and other couriers.

However, Federal Express has established a policy that such shipments cannot be shipped in their Overnight Letter™ Envelopes. Instead, specimens must be packaged for shipment in other approved packages. Shipping in these packages results in a higher shipping charge from Federal Express due to increased handling expense. No exemption had ever been made to that policy. However, we wanted to use the Overnight Letter™ to help keep product costs low. After examining our packaging and subjecting it to a range of tests -- as well as consulting with their medical consultants -- Federal Express granted the first exemption to their policy and granted us permission to use the Overnight Letter.™

Pre-addressed pre-paid Federal Express envelopes would be included in the test kit. Users could either have the packaged picked-up at their door, or drop it off in a Federal Express drop-off box [instructions for calling for the nearest location were included in the test kit]. Additionally, users had the option of sending the sample back via mail. In clinical trials, we established that users could follow directions for shipping and mailing.

4) Are AIDS Home-Test Results Accurate?

Once an adequate specimen has been obtained, a number of research studies have concluded that results will correspond 100% with venipuncture specimens. A number of studies have been conducted which determined that atmospheric conditions, temperature and testing delays will not affect test results. Our clinical trials corroborated that research.

A copy of findings from a study conducted by Johns Hopkins School of Public Health which was published in May, 1987 in the *Journal of Infectious Diseases* is included herein. Our clinical trial data corroborated earlier studies at Johns Hopkins and Data from the National Committee on Clinical Laboratory Standards.

Confirming other research, we noted one very important fact concerning ability to obtain accurate test results once a specimen has been collected. AIDS home-tests must use an ELISA test kit [over 20 such different kits are manufactured] and a confirmatory test which is suitable for use with filter paper. In our research, we found that some ELISA kits would not produce reliable results with filter paper. Our clinical trials demonstrated that the ELISA and confirmatory [Western Blot] tests we did use for clinical trials produced results which correlated 100% with venipuncture samples.

For perspective, our data demonstrated that the particular ELISA and confirmatory [Western Blot] test kits we selected were 100% reliable versus venipuncture. The manufacturer of the ELISA test kit we used in our trials later sought FDA approval for use of their test kit with filter paper [in the laboratory]. On March 7, 1989 that company announced FDA approval saying:

"The filter paper procedure has been used for years to obtain blood samples from newborns for a variety of other tests. This is the first time it has been approved for use in an AIDS test. Presently, the Centers for Disease Control is conducting a series of nationwide screening program on all newborns using this filter paper technique. The National Academy of Sciences has suggested a nationwide screening program on all newborns for the presence of the antibody to the HIV virus."

Although the stability of filter paper has been proven to be reliable for two years, conservatively our packaging was labeled to reflect a one year shelf life.

CORRESPONDENCE

Detecting Antibodies to Human Immunodeficiency Virus in Dried Blood on Filter Papers

COLLEAGUES—Specimens of whole blood dried on filter paper have been used for serological and other screening tests. This method has been used to screen for phenylketonuria [1], hemoglobinopathies [2, 3], antibodies to measles virus [4], and hepatitis B surface antigen [5]. Collecting blood specimens on filter papers is suitable for large-scale screening and for seroepidemiological studies. The dried samples are light, easy to store or mail, cannot be broken or spilled, and take up little space. The major advantage of this technique is the facility with which one can obtain blood samples from finger or heel punctures on infants, children, or others from whom it is difficult to obtain venous blood. We investigated the application of this collection method for detecting antibodies to human immunodeficiency virus (HIV; also known as HTLV-III/LAV).

Thirty-five pairs of coded specimens from patients with AIDS or from hospital staff in Africa were obtained both by venipuncture and by finger stick on filter papers. Serum was separated from whole venous blood and frozen at -70°C for one week, until it was transported on dry ice to Baltimore. Similar paired specimens were obtained (in the First AIDS Service outpatient

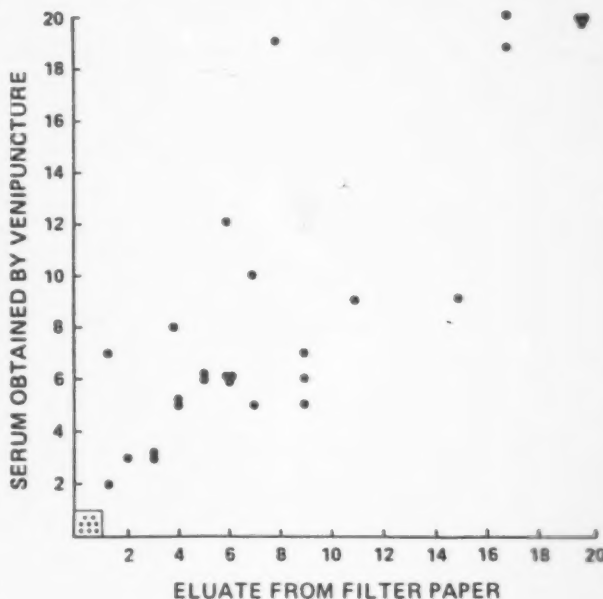
clinic of The Johns Hopkins Hospital in Baltimore) from nine patients known to be seropositive for HIV and from one known to be seronegative. ELISA and western-blot tests were performed on eluates obtained from one circle of dried blood that had been eluted in 0.5 ml of PBS and shaken for 1 hr at room temperature. To clarify the eluates, we centrifuged them at 200 g for 5 min. ELISA tests were performed on the eluates and serum specimens by using commercially available kits, and western blots were performed on prepared immunoblot strips [6].

Filter paper strips (2.5×7.5 cm; 0.96-mm thick) were prepared from sheets of no. 1081-132 filter paper (James River-Rochester, Rochester, Mich). Blood was collected on the filter paper by lancet-induced finger puncture. A fully impregnated disk 10 mm in diameter contains ~ 100 μl of blood [4]. Filter-paper samples were air dried overnight at room temperature, then individually wrapped in plastic wrap and stored at room temperature or in a refrigerator in sealed plastic bags containing silica gel air drier (Davison Chemical, Baltimore).

A specimen was considered positive for antibody to HIV if it was repeatedly reactive on two separate ELISA assays and was confirmed by western blot. The African specimens of serum and whole blood on filter papers were assayed in separate laboratories: ELISA and western blot tests were performed on serum specimens in laboratory A (T. Q.) and on filter-paper specimens in laboratory B (H. F.). In laboratory A, the ELISA kits were from Litton Bionetics, Charleston, SC, and in laboratory B, from ElectroNucleonics, Silver Spring, Md. Western-blot strips were obtained from BioRad, Richmond, Calif. Technicians in each lab-

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Figure 1. Comparison of ELISA test results (ratio index) for antibodies to HIV obtained from serum and filter-paper eluates from 27 African patients with AIDS. Capillary blood was obtained from finger sticks on filter paper, dried, and stored at room temperature for eight weeks. * = Seronegative control ($n = 8$); • = seropositive African patients with AIDS ($n = 27$). The Pearson coefficient of correlation was 0.85 and does not include observations at zero.



oratory were unaware of the serological status of the donors and of the results of testing in the other laboratory. To investigate the effect of drying time at room temperature on the ELISA and western-blot results, we left filter-paper strips obtained from nine patients who were positive for antibody to HIV and who had ELISA ratio index values (ratio index = OD of the specimen divided by the cutoff value) varying from 2 to 15, along with specimens from a seronegative control, at room temperature for two, four, and eight weeks. At the second and fourth weeks, filter strips were refrigerated in a sealed plastic bag with desiccant. All specimens were tested at the end of the eighth week. The eluates were tested by ELISA and western blot after the dilutions were properly corrected.

Agreement of both ELISA and western-blot results from sera and filter-paper specimens was good. ELISA results were totally concordant. One patient had a serum specimen that was positive by western blot and a filter-paper specimen that was negative. The correlation of antibody concentration (as determined by the ELISA ratio index) between sera and filter-paper specimens is shown in figure 1. The Pearson correlation coefficient of 0.85, excluding observations of zero, suggests that filter-paper results reflect those in serum from venous blood over a wide range of concentrations of antibody to HIV. There was no selective loss of any bands on western-blot analysis when blood was properly collected, stored, and shipped on filter-paper strips.

Analysis of specimens obtained from known seropositive and seronegative subjects in Baltimore demonstrated that storing specimens at room temperature for up to eight weeks did not affect the results of testing by either ELISA or western blot. Similarly, the effects of high temperature (37°C), high humidity, and dry conditions (storage in the presence of large amounts of desiccant) were studied on filter-paper specimens stored for three and seven days. These conditions did not affect the results of either the ELISA or western-blot tests, although western-blot bands appeared to be somewhat fainter after specimens had been stored at 90% humidity and at 37°C for seven days. To eliminate the elution step, we directly added whole, one-half, and one-quarter filter-paper disks impregnated with blood to the troughs of the plates, along with the western-blot strip and 3 ml of specimen diluent. The results indicated that even one-quarter of a filter-

paper disk was sufficient to provide results similar to those of eluted dried blood or serum.

These data support the suitability of collecting blood specimens on filter papers for seroepidemiological studies of HIV. Serological results from filter-paper specimens obtained by finger stick are comparable with those from serum specimens obtained by venipuncture. The results were not affected by storage over a few weeks, even at relatively extreme conditions of heat and humidity. This specimen-collection technique will greatly facilitate seroepidemiological investigation of HIV infection in Africa and among populations (such as infants and intravenous drug abusers) from whom it may be difficult to obtain blood by venipuncture.

HOMAYOON FARZADEGAN, THOMAS QUINN, B. FRANK POLK
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5) *Is it Safe to Provide Counseling and Education over the Telephone?*

It should be noted that, as with other aspects of AIDS home-testing, adequate safeguards must be established to ensure that counseling centers are staffed by trained medical personnel and that procedures are established and enforced.

These extended remarks include a portion of our PMA section dealing with counseling. In some cases, identities of individuals or institutions whose comments were meant only for PMA review, and not public disclosure during that process, have not been revealed for purposes of these remarks.

It should be noted that my company's Counseling Center protocol was developed by a psychologist who directs a behavioral research center at a leading university hospital. Further input into development of the Counseling Center was made by the company's medical advisory board which included physicians, psychologists and others with specific experience in AIDS, telephone counseling and crisis intervention. Names and affiliations of these individuals -- most nationally recognized for their work -- were included in our PMA.

Additionally included in this section is a copy of a study on HIV testing published in the Journal of the American Medical Association. In the "Comment" section of that report it is noted:

"Our observations indicate that no standard practice is currently being followed for ordering HIV tests... Only 10% of tests performed fulfilled the criteria for an appropriate test (where the test was indicated and consent and counseling were provided with documentation in the medical record. Education of health care providers about HIV testing alone without enforced guidelines may be insufficient..."

Misuse of HIV testing reported in the Minnesota study included:

" six instances where a positive ELISA result was interpreted by physicians as a positive test, despite a negative finding from Western blot analysis. In five situations, asymptomatic seropositive HIV patients were recorded as having AIDS. In one case, mislabeling of a patient specimen was documented. A positive test result was found in a chart involving an outpatient; no mention of the test was found in the medical record. The patient was contacted and interviewed; he had no risk factors for HIV infection and results of a repeated HIV antibody test were negative. The blood type of the original positive specimen was AB while the patient's blood type was A. A review of the processing of the specimen could not determine how the mislabeling occurred. No high-risk patients were seen that day in the clinic and no other specimens for HIV antibody serology were submitted to the laboratory from the clinic. An intentional mislabeling of the specimen could not be excluded."

devices similar to AIDS CHECK. These products are for measuring whole blood glucose levels. Although used most often by diabetics, these products may also be used by non-diabetics. While many diabetics receive training from their doctors in the use of these devices, a significant number receive no training. Therefore, the experience of untrained people in obtaining fingerstick blood with these products may be relevant to AIDS CHECK. Only the blood drawing step would be expected to be relevant.

However, since the use of specific instructions and illustrations was found to be the single most important factor in determining whether people were able to correctly perform AIDS CHECK, the data on the ability of people to correctly follow blood drawing instructions in other manufacturer's products would not be expected to accurately reflect the ability of people to follow AIDS CHECK instructions.

b) Summary of Studies on Ability of Untrained People to use Home Blood Drawing Devices

Several studies have examined the ability of people without previous experience to perform home glucose monitoring. A review article in 1985 reviewed the literature on problems associated with use of home glucose monitoring tests. Specific problem areas were identified. Difficulty performing fingerstick was not found to be a problem in adults.^{3, 50}

3) EVALUATION OF TELEPHONE COUNSELING

a) History of Telephone Crisis Services

Telephone crisis services have a history dating back to the early 1900's when a 24-hour telephone crisis service was started by the National Save-A-Life League in New York.⁴

In the 1960's, the community mental health movement, bolstered by the Community Mental Health Act responded to the shortage of widely accessible mental health services. A major thrust was providing wide-spread access to mental health care by establishing telephone counseling services across the nation. A study in 1977 estimated that over ten million people a year were being served by over 600 centers.⁴⁰

The Los Angeles Suicide Prevention Center's pioneering efforts established that handling crisis, particularly suicide, over the telephone was not only possible, but perhaps the best method for handling such situations. Particularly noteworthy was the development of the technology for assessing suicide lethality and techniques for responding to people in crisis.⁴

b) The Effectiveness of Telephone Counseling

A number of research studies have evaluated the effectiveness of telephone counseling services. The following summarizes a review of the literature:

1) Telephone Crisis Services

Research evaluating the effectiveness of telephone crisis services has relied on three types of study design. First, studies involving people making simulated client calls to centers and having these simulated clients evaluate the characteristics of the telephone counselor and other services provided. In such studies, the telephone counselor is aware that a study is being conducted, but does not know which of the calls are genuine or simulated. Second, studies evaluating counselor responses to genuine clients. Finally, studies evaluating satisfaction of clients who have used these services.

The results of these studies have generally indicated that callers were satisfied with the services and that counselors were generally found to have high levels of empathy, warmth, and genuineness. Most importantly, Bergen, Lambert and others demonstrated that these results parallel the results of client ratings of therapists in face-to-face counseling.^{2, 43}

Several studies have examined the long term effectiveness of telephone crisis services by contacting callers 48 hours to 12 months after their calls and asking them to evaluate the helpfulness of the service. Results have indicated that approximately 70 percent of the clients rated the service as helpful or very helpful. This is an impressive figure since the results of thousands of face-to-face psychotherapy outcome studies indicate that approximately 66 percent of clients feel that these face-to-face services are helpful or demonstrate improvements on objective variables.⁴⁶ Thus, we can conclude that the results of telephone counseling parallel that of face-to-face counseling.

One of the most important services that crisis counseling provides, whether via face-to-face or telephone counseling, is referral to appropriate community resources. Many studies have examined client follow through of referrals from face-to-face and telephone counseling sessions. Paul and Turner demonstrated that rates of up to 80% of clients following through on referrals given in telephone counseling sessions are achieved when agencies make a specific effort with their counselors to get their clients to reach appropriate referrals.³⁸ Given the fact that up to 50% of clients in face-to-face psychotherapy never return after the first session,⁴ these results for telephone counseling must be considered impressive.

Several studies have compared the suicide rate in communities with telephone crisis services with control communities that do not have such services. While the results are somewhat mixed, several studies have indicated that, "crisis lines may be associated with lower rates of suicide."⁴³

Rosenbaum and Calhoun, in their review of telephone crisis services state:

Intuitively, the concept of a hotline is a good one. It provides a relatively economical method of dispensing health services to greater proportions of the community than can be reached by conventional services... It offers an amenity and freedom from both legal and bureaucratic "red tape" which makes it invaluable in areas such as drugs, sex, birth control, abortion, counseling suicide, and many adolescent problems. The hotline transcends geographical barriers where seconds can make a life or death difference and offers an acceptable form of help to many persons who would not normally come into a helping agency.⁴⁰

2) Radio Psychologists as Telephone Counselors

Research on the effects of calling a radio psychologist on the mental health of callers is relevant to our proposed program because it provides yet another example of a telephone counseling service.

Radio shows generally work in the following way: The caller calls the radio show. A screener answers the call and establishes what the issue or problem is. The caller then waits for the psychologist to answer the call on the air. The caller describes the situation and the psychologist responds. The calls are usually short in length, averaging around five

minutes. The work of the radio psychologist is similar to telephone crisis services in that the caller is anonymous and the service is provided over the telephone.

Studies evaluating the effectiveness of radio psychologists were conducted by researchers from the American Psychological Association's Media Psychology division who asked callers a series of questions both before and after the phone call. Additionally, other research has evaluated the effects of the counseling provided by radio psychologists on well being of the callers. The results have indicated that callers are very satisfied with the services received by radio psychologists. For example, Bouhoutsos, Goodchilds & Huddy found that immediately after the call, 64% of the callers reported feeling better about themselves and showed significant gains on a measure of psychological well-being, as compared to pre-call level of well-being.⁵

3) Expert Opinions on Telephone Crisis Services for AIDS Counseling

Experts in the fields of counseling, telephone counseling, and AIDS counseling were consulted in the development of the AIDS CHECK counseling service. These experts felt that telephone counseling is an effective means of providing initial counseling services to people receiving HIV antibody results. In some circumstances, the telephone was felt to be the best means to provide an initial entrance point into counseling, as it is less threatening for some people than face-to-face counseling.

The following summarizes the opinions of some of these experts:

- [*], Executive Director of the [major suicide prevention center *] expressed the view that, "at the moment of crisis, the telephone is the best source of help." [*] went on to discuss how the anonymity of the telephone provides a tremendous service for people in need, providing them the strength to reach out for help.

Regarding the impact of learning about positive HIV antibody results over the telephone, [*] noted that, "the shock of hearing the positive result, and any potential for increased suicide risk can be effectively handled with good counseling."

The goal of telephone counseling services is often to get the caller

* Note: Complete names of people and organizations appeared in PMA.

into face-to-face, long term counseling. Thus, telephone services are not seen by [*] as a replacement for face-to-face counseling but as part of the process of people reaching face-to-face counseling if needed.

- [*] Project Manager of [a major suicide prevention center *], who is responsible for training counselors who work with AIDS clients, was also consulted. [*] notes that the [receives many calls from people who are concerned about results from AIDS testing, or have other AIDS related fears. [*] felt that the UHL plan to deal with the AIDS epidemic was feasible and went on to add, "I can't think of any other way to do it."
- [*] is a nationally known psychologist and consultant to the [state-wide and supported] AIDS project who is familiar with the status of AIDS counseling. [*] stated that he was not impressed by the quality of counseling given at State Health Department testing centers in an "obligatory 15 or 20 minute contact." [*] felt that such contacts were generally not helpful. More helpful, [*] felt, were referrals for ongoing counseling. In this context, [*] stated that, "I can't see why telephone counseling wouldn't work."
- [*], Director of Counseling and Social Work at the [*] County Hospice was also consulted. As background, many communities around the United States have a local Hospice that provides counseling services to dying people and their families during the last six months of life. As expected, the number of patients with AIDS, and their families, has been increasing at Hospices around the country.

[*] felt that the AIDS CHECK service would be a major asset to the work done by the Hospices because the program impacts potential Hospice clients at the beginning stages of illness. Currently, many clients come to the Hospice at the final stages of their disease, without having received any prior help from a social support service.

By helping HIV positive clients to recognize the importance of seeking out support and counseling in the earlier stages of illness, rather than waiting for the final stages, if and when they reach the Hospice, they will have experienced the benefits of social support for the full duration of the illness and death and dying process. In this

way, [*] feels the AIDS CHECK service will facilitate achievement of the objectives of the Hospice movement.

In summary:

- 1) Studies have indicated that the effectiveness of counseling over the telephone parallels the effectiveness of face-to-face psychotherapy.
- 2) Telephone services allow people to seek help anonymously, thus some people find telephone counseling less threatening than a face-to-face encounter.
- 3) For many, it is much easier to reach for the telephone than it is to make an appointment, go to the appointment, and return for another appointment. Thus, telephone services make mental health services, information, and referral services more widely available.
- 4) Telephone crisis services have been successfully helping people in crisis since the early 1900's. Experts in this field believe that trained counselors can help people cope with the emotional reactions to a positive HIV diagnosis in a telephone counseling session.

* Note: Complete names of people and organizations appeared in PMA.

Analysis of the Use of HIV Antibody Testing in a Minnesota Hospital

Henry, MD; Myra Maki, RN; Kent Crossley, MD

respectively studied the clinical use of human immunodeficiency virus antibody serology at one 450-bed medical center and affiliated clinics from 1985 through August 1986. No restrictions were placed on the use of HIV antibody serology during that time, although it was recommended that consent and risk-reduction information be provided. Testing was performed on 25 (9%) of these were positive. Nearly half (44%) of the patients had no recognized risk factor for HIV infection recorded in their medical records. For an additional 44% of the patients, the test was medically indicated but consent and counseling were not documented. For only 10% of HIV antibody testing as there notation that consent was obtained and that risk-reduction information was provided. These results indicate that HIV antibody testing is being missed and that opportunities to provide risk-reduction information are being missed.

(JAMA 1988;259:229-232)

Human immunodeficiency virus antibody serology has been commonly available in the United States since 1985. The initial practical application of HIV serology was to blood donors for evidence of HIV infection.¹ In an effort to protect the blood supply.^{2,3} Subsequently,

See also p 264.

alternative test sites⁴ were soon established to provide HIV antibody testing to persons in high-risk categories so that these individuals would not be on blood banks to learn their antibody status.⁵

Guidelines for HIV antibody testing in the clinical setting in April 1985, without specific guidelines for its use.⁶ A recent discussion addressed the clinical framework for evaluating antibody testing.⁷ The suggested sites for testing included the individual and supportive care before and after testing and the physician in the acquired immunodeficiency syndrome (AIDS) setting.^{8,9} A consensus regarding recommendations for appropriate clinical HIV serology has not emerged. We note that such guidelines are

needed because of the important medical, psychological, legal, and social implications that a positive test result has for the patient.

Although little published data exists, HIV antibody testing in the clinical setting is far more common than at the alternative test sites; between June 1985 and May 1986, 75% of all nondonor HIV antibody testing in Minnesota occurred in the clinical setting.¹⁰ To characterize the clinical use of HIV antibody serology and to determine how often criteria for appropriate testing are present, we evaluated the use of the test at one institution. Results of our evaluation are presented in this article.

METHODS

All HIV antibody serologies ordered through one medical center from April 1985 through August 1986 were identified from the hospital laboratory office. The medical center is a 450-bed teaching hospital that serves as a regional trauma center and is affiliated with several satellite clinics. All HIV antibody test samples are assigned a code number that is logged with the patient's name and hospital number in the hospital's virology laboratory. The sample is then forwarded to the American Red Cross Blood Services, St Paul Region, for enzyme-linked immunosorbent testing (ELISA).¹¹ Specimens repeatedly reactive by ELISA are then analyzed by Western blot assay¹² and are defined as positive if antibodies to gp41 and p24 bands are present. Results are then sent to the medical center's laboratory, where they are entered into

the laboratory computer and each patient's medical record.

All inpatient, outpatient, and outlying clinic records were reviewed for patients who had HIV antibody serology performed, for purposes other than blood donation, during the study. Age, gender, race, and HIV risk factors were recorded for each patient. The following information pertaining to the HIV antibody test was also recorded: date of the test, results, physician or other health care worker ordering the test (and their level of training), first or repeated test, priority of test ("stat" vs routine), location of origin of sample (inpatient, outpatient, or satellite clinic), and from which service.

Chart notes pertaining to the HIV antibody test were evaluated. Notes were categorized as follows: no note mentioning the HIV test on the day the test was ordered, reason for the test is somewhere in the medical record, test discussed with patient, test and risk-reduction counseling provided, or some form of consent signed by the patient. Tests performed only for reassurance (no medical indication) at the patient's request and employee exposure evaluations were analyzed separately.

In addition, appropriateness of the testing was evaluated using criteria developed by the Minnesota Department of Health.¹³ The appropriateness category of each test was determined according to the following criteria: (1) the test was indicated because the patient was in a high-risk category or had clinical symptoms compatible with possible HIV infection, (2) patient consent was obtained before the test was performed, and (3) counseling about the test and risk-reduction information were provided. In 11 cases, information was incomplete and appropriateness could not be evaluated.

The previous information for each patient was tabulated on a form and assigned a study number. Statistical significance was determined by standard univariate analysis.¹⁴

RESULTS

Demographic Data

Results were available for all 275 patients who had HIV antibody serology

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ordered during the study period; 25 (9%) were positive. The patient's race could be determined in 240 cases. One hundred ninety-three (80%) were white, 35 (14.6%) were black, and 12 (5%) were Asian, Hispanic, or Native American. The gender could be determined in 270 cases. One hundred seventy-eight patients (65%) were men; 25 of these (14%) had positive test results. All men with positive test results were between the ages of 16 and 49 years. None of the 92 women tested had positive results.

Two hundred sixty-four patients (96%) had medical charts from which HIV infection risk group data could be determined (Table 1). One hundred forty-seven patients had at least one recorded risk factor (56%); 23 of these patients were seropositive (16%). One hundred seventeen patients (44%) had no risk factors noted in their medical record; two (2%) of these patients were seropositive. The seropositivity rate for patients with no recorded risk factor (2%) was significantly lower than the rate for patients with one identifiable risk factor (16%) ($P < .001$).

Level of Training of Health Care Professional Ordering the HIV Antibody Serology and Clinical Site of Testing

For 243 tests, the health care professional ordering the test could be determined. The number of tests ordered and the rate of seropositivity by level of training for the person ordering the test were as follows: staff physicians ordered 117 tests, 8% were seropositive; house staff ordered 104 tests, 13% were seropositive; nurses ordered 14 tests, none were seropositive; and medical students ordered seven tests, none were seropositive.

Location

The site where the test was ordered could be determined in 264 cases. One hundred forty tests (53%) were ordered from hospital outpatient sites; 15 (11%) of these results were positive. Ninety-eight (37%) tests were ordered from inpatient services; six (6%) test results were positive. Twenty-six tests (10%) were ordered from satellite clinics; three (12%) of these results were seropositive. The site of patient interaction could not be determined in 11 cases and one positive result was identified from that group.

HIV Antibody Serology by Service

Information about the service ordering the test was available for 258 cases (Table 2). Medicine and surgery subspecialty services were combined in this summary, but more than 20 different specialties contributed to the total.

Table 1.—Risk Categories of Patients Tested for Human Immunodeficiency Virus Antibody

Risk Group	No. (%) of Patients Tested (N = 264)	No. (%) of Positive Test Results
Homosexual/bisexual men	46 (17)	17 (37)
Homosexual/bisexual men and intravenous drug abuser	10 (4)	2 (20)
Intravenous drug abuser only	66 (25)	2 (3)
High-risk partner	22 (8)	1 (4.5)
Hemophilic	3 (1)	1 (33)
No risk behavior identified	117 (44)	2 (2)

Table 2.—Human Immunodeficiency Virus Antibody Testing by Clinical Service

Service Ordering	No. (%) of Tests Ordered* (N = 258)	No. (%) of Positive Results
Medicine	94 (36)	13 (14)
Emergency department	28 (11)	1 (3.5)
Psychiatry	28 (11)	1 (3.5)
Family practice	27 (10)	2 (7)
Surgery	25 (10)	3 (12)
Employee health	22 (8)	0 (0)
Gynecology/obstetrics	14 (5)	0 (0)
Pediatrics	9 (4)	1 (11)
Neurology	4 (2)	0 (0)
Dermatology	3 (1)	2 (66)
Dental	2 (1)	0 (0)
Workhouse	2 (1)	1 (50)
Could not determine	17 (6)	1 (6)

*Percent of total tests ordered by that service.

†Percent of tests ordered by that service that had positive results.

Table 3.—Human Immunodeficiency Virus-Related Notes in Chart by Major Risk Group

Type of Note	No. (%) in Risk Group			
	Homosexual/Bisexual Men (n = 46)	Homosexual/Bisexual and Intravenous Drug Abuser (n = 16)	Intravenous Drug Abuser (n = 66)	High-Risk Partner (n = 22)
No chart note	13 (28)	5 (30)	26 (39)	3 (14)
Reason for test somewhere in chart	34 (74)	6 (38)	40 (61)	18 (82)
Test discussed	19 (41)	2 (12)	15 (23)	10 (45)
Test and risk reduction discussed	11 (24)	0 (0)	3 (4.5)	7 (32)
Signed consent or consent form	3 (6)	0 (0)	2 (3)	1 (4)

Notes in Record Pertaining to HIV Antibody Test

A chart was available to review for 264 tests. A rationale for the test was noted in 154 (58%) of the charts. For 108 patients (41%), the HIV antibody test was not mentioned in the progress note on the day when the test was ordered. Notation that the test was discussed with the patient was present in 54 charts (21%). Documentation that discussion of the test and risk-reduction counseling occurred was present in 24 charts (9%). A patient-signed consent was present in eight (3%) of the records. The notes in the chart by risk activity and service are shown in Tables 3 and 4, respectively. Patients who had HIV antibody testing ordered while on surgical services (84%) were more likely

than those on a medicine service (34%) to have no note in the chart referring to use of the test ($P < .001$).

Appropriateness of HIV Antibody Test

Table 5 summarizes the appropriateness categories to which 264 patient tests could be assigned. No medical or other indication was determined for 48 patients (19%). Only 25 (10%) of the tests could be classified as fully appropriate. Appropriateness of testing did not vary by gender, race, or level of training of the care provider ordering the test.

Outpatients (from hospital or satellite settings) were more likely (24 of 125) to have appropriate consent and counseling than inpatients (one of 98) ($P < .0001$). Also, an inpatient was more

likely (26 of 86) to have a test with no indication than was an outpatient (20 of 86) ($P < .05$). Patients seen by a medical service (14 of 94) were more likely to have an indicated test and adequate counseling than were surgery patients (none of 25) ($P < .0001$). A patient with an indicated test and a positive test result (seven of 25) was more likely to have appropriate consent and education than a patient with an indicated test but a negative result (18 of 90) ($P < .05$).

Chronology of HIV Antibody Test Ordering

For the study period, a month-to-month analysis of testing patterns was performed (Figure). No significant change over time in documentation in the patient's medical record regarding the appropriateness of the testing performed was noted.

Misuse of HIV Antibody Test

A review of all tests ordered documented numerous questionable uses of the test. Eleven patients were identified for whom no details were recorded in the chart about who ordered the test or why the test was ordered. In six instances, a positive ELISA result was interpreted by physicians as a positive test, despite a negative finding from Western blot analysis. In five situations, symptomatic seropositive HIV patients were recorded as having AIDS.

In one case, mislabeling of a patient specimen was documented. A positive test result was found in a chart involving an outpatient; no mention of the test was found in the medical record. The patient was contacted and interviewed; he had no risk factors for HIV infection and results of a repeated HIV antibody test were negative. The blood type of the original positive specimen was AB while the patient's blood type was A. A review of the processing of the specimen could not determine how the mislabeling occurred. No high-risk patients were seen that day in the clinic and no other specimens for HIV antibody serology were submitted to the laboratory from the clinic. An intentional mislabeling of the specimen could not be excluded.

COMMENT

Ethical and technological issues relating to HIV antibody testing have been widely discussed.¹⁰ In contrast, little information has been published about the manner in which this new technology is used in clinical practice. We believe it is important to determine how HIV antibody serology is being used by clinicians and whether a need for additional guidelines exists. That a

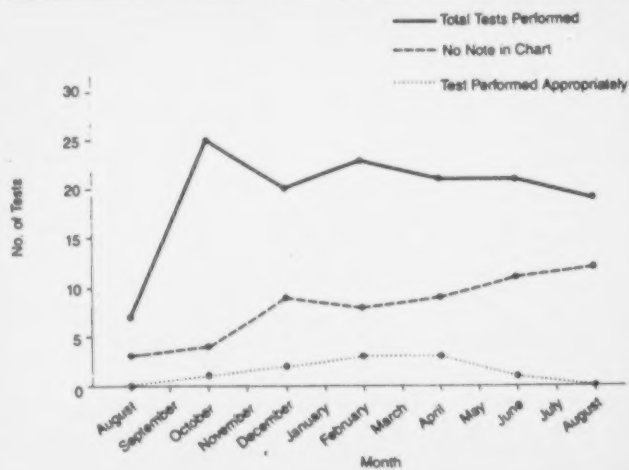
Table 4—Contents of Note in Chart Pertaining to Human Immunodeficiency Virus Antibody Test

Service*	No. (%) of Patients				
	No. Note	Reason Noted	Test Discussed	Test/Risks Discussed	Signed Consent
Medicine (84)	32 (34)	81 (85)	27 (29)	14 (15)	7 (7)
Emergency department (28)	9 (32)	19 (68)	3 (11)	1 (4)	0 (0)
Psychiatry (26)	17 (61)	12 (43)	2 (7)	1 (4)	0 (0)
Family practice (27)	5 (18)	20 (74)	14 (52)	4 (15)	0 (0)
Surgery (25)	21 (84)	5 (20)	0 (0)	0 (0)	0 (0)
Employee health (22)	13 (59)	11 (50)	0 (0)	0 (0)	0 (0)
Obstetrics/gynecology (14)	3 (21)	11 (79)	4 (29)	2 (14)	1 (7)
Pediatrics (9)	3 (33)	6 (66)	1 (11)	1 (11)	0 (0)
Neurology (4)	1 (25)	2 (50)	0 (0)	0 (0)	0 (0)
Dermatology (3)	1 (33)	2 (66)	1 (33)	0 (0)	0 (0)
Dental (2)	2 (100)	0 (0)	0 (0)	0 (0)	0 (0)
Workhouse (2)	1 (50)	1 (50)	1 (50)	0 (0)	0 (0)
Unevaluable (17)	...	...	...	...	...

*Number in parentheses indicates number of patients tested by service.

Table 5—Appropriateness of Human Immunodeficiency Virus Antibody Testing

Category	No. (%) of Patients
Test indicated, consent obtained, and risk-reduction information given	25 (19.5)
Test indicated, consent obtained, but no risk-reduction counseling documented	25 (19.5)
Test indicated, risk-reduction information provided, and no consent obtained	1 (4)
Test indicated, consent not obtained, and no risk-reduction counseling documented	117 (44)
Test not indicated, no consent obtained, and no risk-reduction information documented	49 (18.6)
Reassurance indications	
Consent and counseling documented	8 (3.4)
Consent and risk-reduction counseling not documented	7 (2.7)
Exposure evaluation	31 (11.7)
Total	264 (100)



Pattern of human immunodeficiency virus antibody testing at Minnesota hospital from August 1985 to August 1986

new blood test can be cast in the role of a controversial new technology has occurred previously. The introduction of the Wassermann test for syphilis in 1906 led to considerable debate in both the public health and the clinical arenas.²⁰

The data presented in this article are from a medical center in Minnesota, a state where the incidence of HIV infection is relatively lower than in some areas of the United States. Also, there are no legal restrictions on the use of HIV antibody serology in our state. This situation is similar to that in many areas and, therefore, we believe, our data may reflect the clinical practice in other geographic areas also.

These data demonstrate that the HIV antibody test is being ordered by physicians in a variety of medical specialties with a range of medical training. Our observations indicate that no standard practice is currently being followed for ordering HIV antibody tests. In 44% of the tests performed, the patient had no recognized risk factor for acquiring HIV infection (Table 1). In an additional 44% of tests performed, the test was medically indicated but patient consent and counseling were not documented in the medical record (Table 5). Only 10% of tests performed fulfilled the criteria for an appropriate test (where the test was indicated and consent and counseling were provided with documentation in the medical record).

Education of health care providers about HIV testing alone without enforced guidelines may be insufficient to change ordering patterns. During the period encompassed by this study, the health care providers at St Paul-Ramsey Medical Center were exposed to broad education about AIDS and HIV testing (1100 hospital employees attended a series of AIDS lectures; numerous memoranda to staff physicians; and multiple AIDS- and HIV testing-related conferences for medical students, house staff, and staff physicians). However, as shown in the Figure, no significant change in the appropriate use of the HIV antibody serology occurred over time. Since physician participation in such education efforts was not universal, programs providing key information to clinicians ordering HIV antibody serology need to be developed.

An important issue frequently confronted is whether the HIV antibody test should be treated differently from other patient tests. For example, hepatitis B serology is routinely obtained from many hospitalized patients without their specific consent if an indication exists (ie, employee needlestick). Informed consent is a complex issue,²¹ especially in the context of HIV antibody testing. Vexing situations, such as

when a patient refuses to provide consent for HIV serology when the physician thinks it is necessary (medically or for evaluation of exposure), are encountered frequently. Several states have restricted use of the HIV antibody test by limiting transmission of test results or by developing formal consent forms. Some institutions have developed policies restricting use of HIV antibody testing to designated physicians or to situations in which specific criteria have been satisfied. The wide range of approaches employed nationally, in addition to our data, clearly suggests that standardized guidelines need to be developed and disseminated to physicians.

In lieu of such guidelines, we would make the following recommendations. First, the reason for ordering HIV serology and the patient's consent need to be clearly documented in the chart. Second, health care workers need to be further educated about the appropriate use of HIV serology and its role in clinical medicine. Third, clinicians can perform a valuable public health as well as medical service by optimal use of HIV antibody testing. Counseling high-risk seronegative patients on risk reduction is potentially extremely valuable but, in our experience, is not done routinely in clinical settings. Hospitals should develop policies whereby HIV antibody testing is obtained with patient consent and in conjunction with risk-reduction counseling. Coupling testing with consent and counseling avoids complex ethical and legal questions and may enhance the value of either a positive or a negative test result.

We expect that institutions nationwide, with wide variation, will report experiences with HIV antibody testing that are similar to ours. Our data highlight the debate on how the needs of clinicians and institutions pertaining to HIV antibody testing need to be interfaced with the guidance provided by government agencies. Recent reports, from both the United States and England, suggest that the attitudes of clinicians regarding HIV testing may differ from the opinions expressed by experts in public policy statements.^{22,23} A community consensus involving public health officials, local medical associations, and hospital associations needs to be reached. Endeavors to minimize the reasons for caution regarding HIV testing (ie, insurance, employment, and confidentiality issues) may facilitate the use of the HIV antibody test as a clinical and public health tool in combating the spread of AIDS.

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BENEFITS

1) Only Testing can Provide Knowledge

Public health officials agree that AIDS testing should be widely available. We substantiated this in some detail in our 1987 premarket approval application, and I will quote a very short passage:

"For example, Dr. C. Everett Koop, the U.S. Surgeon General has stated that, 'Every woman in the country considering pregnancy should be tested for AIDS.* And, at the June, 1987 meeting of the American Medical Association, the AMA adopted the following recommendation: 'Tests for the AIDS virus should be readily available to all who wish to be tested. The tests should be routinely subsidized for individuals who cannot afford to pay the cost of their test.'"

The exact number of HIV infected individuals is not precisely known. It is recognized that most people who are carrying the HIV virus do not know they are infected since there is an incubation period after infection and before symptoms begin. According to Bob Byers, chief of AIDS statistics at the CDC, quoted in a 13,1989 issue of *Barron's* magazine:

"The length of the incubation period goes up every year, and the longer the incubation period, the more people have to be infected just to generate the number of AIDS cases we see now."

It should be added that there is limited data on sexual behavior change in the face of AIDS -- not only on AIDS testing but also on condom use. Public education efforts have generally not emphasized the importance of seeking testing; rather they have emphasized the need for using a condom, and other "safe sex" precautions, when HIV status is not known.

Research which has studied sexual behavior change focuses on condom use. Although condom sales have increased by almost 100% in the last four years, there is now an increasing awareness that sexual behavior has not changed significantly. Mathilde Krim, co-founder of the American Foundation for AIDS Research recently observed in a *Barron's* magazine article on AIDS:

"There is 100% awareness of AIDS, but below the surface -- in private behavior -- there is very little change. The rubber manufacturers report sales way up for rubber gloves, rubber aprons; in instances when gloves and aprons are appropriate, there is ironically very little risk, but in public, we go through the motions. When it comes to intimate life, we change very little."

Additionally, it should be noted that a "Sounding Board" article in the May 21, 1987 issue of *The New England Journal of Medicine* entitled, "What is Safe Sex?"

which discussed "safe sex" in depth a section entitled "Safe Sex without Testing or Standards, observed:

" 'Lower' risk, however, is the most that traditional safe-sex counseling, exhortations, and written handouts have achieved. Every communication, for example, stresses the need to avoid (but not necessarily eliminate) anal sex. But even among the highly educated and motivated cohort of homosexual men whom my colleagues and I have studied in New York City and Washington, D.C., 48 percent continued to have anal sex in 1986 (unpublished data).

The author, James J. Goedert, M.D. from the National Institutes of Health went on immediately to observe about the effectiveness of condoms:

"Much recent emphasis has been placed on condoms, and there is little doubt that meticulous use of condoms can reduce the transmission of HIV. However, 77 percent of the men in our studies who practiced anal sex in 1986 did not use condoms (unpublished data). Furthermore, it has recently been shown that condoms failed to prevent HIV transmission in 3 of 18 couples, suggesting that the rate of condom failure with HIV may be as high as 17 percent (and Fischl MA; personal communication). It is clear that the use of condoms will not eliminate the risk of transmission and must be viewed as a secondary strategy."

2) Home Testing will be Utilized

Existing AIDS testing services are not adequate for a number of reasons. As we stated in our premarket approval application:

"In summary, there is general agreement by government and health care personnel about the urgency of making AIDS education, testing and counseling available to everyone in the United States. To date, efforts to accomplish this have not succeeded. This failure is due to a variety of factors:

- 1) There are insufficient state, local and federal funds to set up enough testing centers at convenient locations, open during convenient hours, to be easily accessible by everyone.
- 2) Many people do not wish to use existing counseling, education and testing resources because of inconvenience, embarrassment, or fears about confidentiality.
- 3) The availability and quality of counseling and educational services at testing facilities is highly variable."

Again, quoting from our premarket approval application:

"Studies to determine the reasons people do not get tested were conducted at the University of California at San Francisco by Coates, Morin & McKusick, who identified a high risk sample of approximately 500 bisexual and homosexual men. Over the course of two years, only about 40 percent had been tested for AIDS. Their studies showed that major barriers to taking the AIDS test included desire for confidential testing and concerns about discrimination."

Our PMA went on to discuss a survey conducted in conjunction with our clinical trials in which 33% of 136 people surveyed said,

"that if they were concerned about having AIDS, they would *not* go to a physician or county health department to obtain an HIV test because of fears that confidentiality would not be maintained and would only get tested using a home AIDS test like AIDS CHECK... 60% said that if they were concerned about having AIDS, they would prefer to use AIDS CHECK. Convenience was a frequently cited reason."

Testimony of Dr. Donald Berns of the New York State Department of Health,
Wadsworth Center for Laboratories and Research, Albany, New York, before
the Congressional Subcommittee on Regulation and Business Opportunities

March 23, 1989

A very substantial amount of the health care cost in the USA derives from medical testing services. The exact percentage may be between five and ten percent. In New York State, we have a very active program that regulates a substantial part of this activity, the clinical laboratory testing environment, and assures high quality testing. This result is achieved by a combination of the State Public Health Laboratory's diligent program of laboratory evaluation and education, which has resulted in cooperation in positive regulatory interactions that is helpful to the professional participants as well as to the public.

Beyond cost, however, our overall motive is to provide assurance to the public that the medical testing services are of the high quality sufficient to contribute to their course of health care.

There are two parts of medical testing services that go beyond the traditional clinical laboratory testing environment. One is the mobile medical laboratory (most commonly seen in health fairs) and the other is the public's use of home test kits. Let us deal with the mobile laboratory first since this activity is also regulated under our Clinical Laboratory Evaluation Program.

We encounter many activities that are of great potential danger to the unsuspecting public and that our regulations are designed to prohibit. Here are a few examples. Recently a company that markets fish oil capsules rented a ballroom at a major metropolitan hotel to conduct a health fair with free cholesterol testing for the public. We were told the purpose of this company's fairs as conducted throughout the United States was to encourage the selling of fish oil capsules to be used in the promised reduction of cholesterol. When the company was confronted with our regulations, which prohibit such activities, except under strict guidelines, we were told about the costs already incurred (thousands of dollars for rental, equipment etc.) and finally received a phone call from an individual identifying himself as a NY State licensed physician who asserted that all persons arriving at the fair were his patients. He also volunteered that a good cholesterol level was 100 mgs/dL plus your age. (This is strikingly similar to blood pressure parameters and is bound to be good for fish oil capsule sales since levels as high as 240 mgs/dL are most often considered as normal.) In a second situation, a major union organization wanted to conduct a fair in which the responsible physician only wanted to be informed of cholesterol levels above 900 mgs/dL.

It is to protect the public from such abuses that the NY State program allows mobile laboratory or health fair types of testing only under very specific guidelines. The following criteria must be followed in all such programs:

1. The testing method/technique must be of documented accuracy and reproducibility.

2. The screening must identify a treatable disease or a condition of public health significance which is preventable by early detection. The affects of erroneous results must be considered.
3. All testing must be conducted under the active supervision of a clinical laboratory which possesses a permit in the specific area of testing.
4. The clinical laboratory will be responsible for ensuring that all quality control/quality assurance procedures are followed and that all applicable sections of our regulatory rules are followed.
5. A physician must order all tests and take responsibility for assuring that those with abnormal/at-risk results are appropriately counseled and/or referred to a physician.
6. Procedures must exist to refer participants to a physician if they do not have a personal physician.
7. The screening site must be appropriately located and organized to assure orderly flow. Further, the discussion of results, under the direction of the responsible physician, must take place in an area where the participants can be counseled confidentially.
8. When appropriate, the target groups must be carefully defined to assure that those people for whom the screening is of value are the ones identified and tested.
9. When appropriate, physician education must be provided.
10. Appropriate procedures for safe collection and disposal of specimens must be in place.

In general, items (1) and (2) which deal with testing methodology and treatable disease status are determined by the NY State Department of Health. The balance of the items which deal with actual conduct of the screening are the responsibility of the sponsoring organization and/or the clinical laboratory as part of a formal application for a mobile collection site. The application is processed with a quick turnaround time (a week or so), and once a protocol has been approved additional test sites may be requested.

Currently we process more than 300 applications for health fairs per year and there is a minimum of discomfort for the health fair operators once they understand the regulatory climate, and a large number of regulated health fairs take place on a weekly basis. Stable professional and voluntary organization relationships are fostered and the public appears to be well served. Groups interested in pursuing health fair operations for reasons of exploitation and not legitimate public health concerns are quickly discouraged. This is a dynamic environment in which regulations and laboratory procedures are constantly reviewed by professional staff.

The primary purpose of these standards is to assure that test results

from health screening programs or health fairs are as accurate and reliable as results obtained under properly controlled circumstances in the clinical laboratory environment. If such standards are not adhered to, screening programs could cause unnecessary alarm amongst participants and add to their costs for unnecessary follow up expense. Furthermore, in the absence of standards, individuals are at a higher risk for life threatening misdiagnosis.

The problem of home testing kits such as those proposed to detect the AIDS-HIV virus is much more vexing since current and foreseeable state regulation will not hold the public harmless from the introduction of such testing. The HIV-antibody screening test which is based upon ELISA (Enzyme Linked Immuno-sorbent Assay) or Latex Agglutination technology is an example of the finest technical accomplishments of the biomedical technology revolution. This technique and related techniques have been applied to faster and simpler testing in a variety of testing environments that lend themselves to the appearance of do-it-yourself home testing or doctor's office testing by untrained personnel. None of this technology is fool proof. All of it is subject to the same short-comings of sloppy laboratory procedures, outdated test reagents, inappropriate storage conditions, inability to follow specific instructions as well as unfamiliarity with the expected result for a positive or negative result.

The recently FDA licensed Cambridge Bioscience Latex Agglutination HIV Antibody Kit marketed by a unit of Baxter International is excellent technology and is highly accurate in the hands of well trained laboratory technicians who perform large numbers of these procedures. In less expert hands it has given false results. In literature provided by the company, the test kits used in a physician's office on 102 people screened 10 as repeatedly positive who were all negative on Western blot confirmation. Even in an emergency room, eight of 53 people repeatedly tested positive with the five minute test but only one was confirmed as being infected. The same test performed by personnel skilled in the use and with high test volume has rates similar to the ELISA test. These are just indications of the inability of not necessarily unsophisticated, but relatively untrained, low volume users to perform an excellent test reproducibly. What can we expect from the general public from use of similar tests in a home environment?

It is then necessary to add to this problem the need to confirm the test by Western blot. What assurances do we have this will occur? What kind of counseling can we have for person's that self test? In the current situation we can not be certain that the test available for physician's office use is not being used without Western blot confirmation or that the patient is not being informed of the screening results.

There are few if any convincing arguments for availability of home testing for HIV antibody. In New York State, the state with the highest incidence of AIDS and HIV infection, it is considered a public health imperative to offer free HIV testing that is professionally performed and has as an essential element pre-test counseling and post-test counseling. Testing is only important when accompanied by appropriate counseling for both the uninfected and HIV infected person. The only thing that approaches a vaccination against HIV infection for the uninfected person is appropriate

information. The only treatment which can be offered for the HIV infected individual begins with counseling at the same time the person is informed of the HIV antibody result. Privacy and anonymity is afforded in anonymous testing programs. Economy of testing is not an issue since it is a public health necessity to have the availability of free anonymous testing. Convenience is not an issue since even with the home testing a confirmatory test is an absolute necessity prior to reaching a decision about a positive result. The testing technology in the home environment is an extreme problem, the inability to guarantee counseling is a problem that could well lead to suicides.

In our laboratory we perform more than 600,000 HIV antibody tests per year on specimens from populations with high and low prevalence and maintain an extensive proficiency testing program for all blood banks and related laboratories permitted to perform HIV testing. We have extensive experience with all types of ELISA, Western blot, antigen and related HIV test products. More than twenty five thousand Western blots have been performed. Our observation is that Western blot testing is still an absolute necessity for confirming a positive result, no matter how intense the response is on a screening test. In addition there are a significant number of persons in the population who give strong positive reaction on the ELISA and other screening tests but who are Western blot negative. These persons continue to test ELISA positive, Western blot negative repeatedly. There is another group that tests positive on the screening test and is equivocal or indeterminate on the Western blot and remains in this status. Each specimen tested in the Western blot protocol in our laboratory is treated with the same care as a research specimen. This testing technology is excellent and more closely scrutinized than any other clinical laboratory testing, but it requires skilled professionals to implement and interpret.

Experience with the difficulty of dealing with HIV antibody testing in a well controlled laboratory environment that does a larger volume and more varied volume of HIV testing than anywhere else in the US leads to the inescapable conclusion that home HIV antibody testing could well lead to a new public health crisis of additional morbidity and mortality related to the introduction of home testing kits.



STATE OF FLORIDA
DEPARTMENT OF HEALTH AND REHABILITATIVE SERVICES

TESTIMONY OF PATRICIA A. JOHNS, PH.D.
FLORIDA DEPARTMENT OF HEALTH AND REHABILITATIVE SERVICES
OFFICE OF LICENSURE AND CERTIFICATION
BEFORE THE HOUSE COMMITTEE ON SMALL BUSINESS
SUBCOMMITTEE ON REGULATION AND BUSINESS OPPORTUNITIES

Cholesterol Screening

March 20, 1989

Two laws containing public health measures were passed in Florida in 1949: (1) the clinical laboratory law and (2) the premarital/prenatal syphilis testing law. Prior to passing the clinical laboratory law, anyone could perform laboratory tests. There were numerous people collecting specimens from drug stores and other designated locations and performing the laboratory tests in their homes. One of Florida's major industries, in 1949 through the present is its large tourist population. In the winter the elderly migrated to the warmer areas; in the summer, a younger crowd appeared. Visitors from South and Central America came year round... many of whom were here for diagnosis and treatment of diseases. There were numerous records of erroneous laboratory reports which led to the legislation regulating Florida laboratories.

The 1949 law applied only to independent laboratories and persons employed in them. Hospital laboratories were exempt. It was assumed that these laboratories were more closely supervised and employed better qualified personnel. This law, with some modifications remained in effect until 1967 when the Bureau of Health Insurance (now Health Care Financing Administration)

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BOR MARTINEZ, GOVERNOR

GREGORY L. COLER, SECRETARY

published regulations for independent laboratories seeking reimbursement for tests performed on Medicare patients. Chapter 483, F.S. was changed at this time to include all clinical laboratories and all clinical laboratory personnel. The state law was drafted to parallel the Medicare regulations, except for personnel requirements, so that two standards for quality control and records would not exist. More recently in 1985, personnel standards were upgraded to match the federal regulations so that differences appeared only at the technologist level. The current law authorizes examination of laboratory personnel in licensed facilities and annual inspection of each licensed laboratory. All laboratories must be licensed except those operated by the federal government, those involved in teaching and research and those operated by no more than five physicians for their own patients.

In the administration of the law and the rules, Florida has held many hearings related to personnel licensure, laboratory licensure, administrative penalties and unsatisfactory proficiency testing. In recent years the state has experienced problems with unconventional "screening" facilities some of which were mobile but the cholesterol "screening" issue is the first real "challenge" to the law in its 40 year history. The state has filed an injunction against one of the mobile cholesterol screening companies who ignored a cease and desist order. The following quotations from the law are supportive of our position:

(1) The definition of a clinical laboratory under s. 483.041 is:

"Clinical laboratory means a laboratory where examinations are performed on materials or specimens taken from the human body to provide information or materials for use in the diagnosis, prevention or treatment of a disease or the assessment of a medical condition".

(2) s. 483.091 further states:

"No person shall conduct, maintain or operate a clinical laboratory in this state except a laboratory which is exempt under 483.031 unless a license therefor has been obtained from the department."

(3) s. 483.141 states:

"No person shall conduct a clinical laboratory examination or report the results of such examination unless he is licensed under this part to perform such procedures."

The Florida Department of Health and Rehabilitative Services' legal staff is of the opinion that these sections of Chapter 483, Florida Statutes prohibit testing of any type without proper licensure.

The first cholesterol screening company appeared in Florida in early March of 1988. Our office received numerous calls of protest from clinical laboratories and equally as many calls from people who wanted to start a

similar business. Approximately 20 cease operation letters have been sent from the department to all who were performing tests without a license. This resulted in an injunction being served on the one of the companies.

The other companies were not issued injunctions. The outcome of the one case will serve to determine future activities of all mobile units. We do not know how many mobile laboratories are operating in Florida since they appear to spring up overnight.

The screening companies assert that they are not clinical laboratories, are not performing laboratory tests and are not diagnosing a condition or disease. However, they do state that they measure cholesterol. Some of the advertisements also offer triglyceride and glucose tests as part of their services.

Concerns of the Office of Licensure and Certification about screening operations are:

1. How do they obtain instruments specified by the Food and Drug Administration as instruments to be sold to professional persons or organizations?
2. How can they be sure that their instruments are calibrated?
3. Are non-professionals aware of the importance of quality control and other testing aspects that can lead to erroneous results?

4. Are company representatives aware of community resources available to people who should have consultation and are they providing that information to those they test?
5. Are non-professionals aware of potential infection hazards to the public and to themselves in handling and disposing of blood saturated materials?
6. Are they and their organizations easily traced and identified?
7. What follow-up is provided when abnormal results are obtained?

Considering all of the possible sources of error, lack of consultation, no pretense of follow-up activity, lack of records, release from obligations of infections and erroneous reports, is the public getting accurate test results from the street, mall and flea market hucksters who are totally unregulated?

Some measure of regulation is expected in the next legislative session in Florida. It is anticipated that the laboratory field will demand that all types of instrument testing be confined to licensed clinical laboratory personnel and that non-instrument tests (qualitative screening) be limited to professional personnel in other disciplines, such as nurses, pharmacists and possibly dieticians.

Many hospitals and licensed laboratories are now offering cholesterol screening to the public and, ideally, these are the facilities that should be providing this service to the public.

AIDS ANTIBODY TESTING

March 20, 1989

On a more recent note the comprehensive AIDS law, was passed in Florida in July 1988, requires informed consent including pre- and post-test counseling for the HIV antibody test, that all tests be performed in a licensed lab and provides for confirmatory testing prior to reporting of positive tests.

Periodically, the Florida AIDS Program Office has become aware of groups or individuals advertising "quick" HIV antibody test results or home testing. Although reports of these incidents have been few, there is a potential for a flood of entrepreneurs to provide these "confidential/anonymous, quick tests".

Section 381.609(4)(c), F.S. requires that all laboratory procedures be performed in a laboratory licensed under the provisions of Chapter 483, F.S. This would prohibit the use of any test conducted in a physician's office, unlicensed, mobile lab, or home.

The State Health Office is also concerned about the possibility of including HIV-antibody testing in a mobile testing unit. Extensive pre- and post-test counseling on risk reduction and behavior modification is required by section 381.609, F.S. This counseling is intended to be

provided by a health care provider knowledgeable in HIV/AIDS transmission and prevention. The quality and effectiveness of the counseling in a mobile testing unit could be highly questionable.

Florida has established a very comprehensive counseling, testing and partner notification program providing confidential or anonymous HIV-antibody testing in its 67 HRS county public health units. In addition, voluntary partner notification of the sex or needle-sharing partners of seropositive individuals has resulted in a high positivity rate among partners. Because partner notification is only provided through the HRS county public health unit's sexually transmissible disease program, this effective mechanism for informing contacts of their extreme risk of contracting the virus would not be present for individuals receiving test results from mobile lab personnel.

Because the HIV epidemic is still unfolding, it is vital that epidemiological and demographic information be analyzed. Mandatory reporting is only required for diagnosed AIDS cases, not incidence of HIV infection. However, demographic and epidemiological information is maintained on all HIV tests run in the state labs. In 1988, this totaled over 81,000 cases. Access to such important information would be limited if tests were run in labs other than those included in the current system.

REPORT OF
THE STUDY COMMITTEE
ON CHOLESTEROL SCREENING

FEBRUARY 1, 1989

ACKNOWLEDGEMENT

The Committee would like to acknowledge the incorporation of many of the recommendations concerning cholesterol screening, made by the National Heart, Lung and Blood Institute Workshop on cholesterol screening and the American Heart Association.

We would also like to acknowledge the professional preparation of this report by Ms. Kimberly Stephens of the HRS Chronic Disease Program.

EXECUTIVE SUMMARY

The purpose of this Report is to discuss whether cholesterol screening should be made more readily available to the citizens of Florida and if so, how it can be done safely and accurately.

Much has been learned in recent years concerning the connection between elevated blood cholesterol and coronary artery and other vascular diseases. Blood cholesterol is a major contribution to these diseases. The public is quickly learning this and demanding cholesterol screening. In light of this new knowledge and increased demand for testing, the Committee concluded that cholesterol screening should be made more readily available to the extent that it can be performed safely and accurately.

This Report recommends detailed standards for the testing instruments, personnel, level of supervision, quality assurance, counseling, education, referral and follow-up.

The Committee felt strongly that if these minimum standards could not be followed, screening should not be done.

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INTRODUCTION

In recent years accumulating medical evidence has convinced the international scientific community that coronary artery and other vascular diseases are associated with elevated levels of blood cholesterol. Furthermore, it would appear that lowering the cholesterol level may favorably influence the evolution and/or progression of these diseases which cause almost one million deaths per year in this country. This evidence persuaded the National Heart, Lung and Blood Institute (NHLBI) to assemble scientific leaders to review the evidence, reach a consensus, and make recommendations to the medical community and society at large. The scientists concluded that the generally accepted "normal levels" for the blood cholesterol of the American public are pathologically high. Furthermore, they emphasized that the significance of a given cholesterol value depended in part on the presence or absence of easy to identify risk factors in the individual. The scientists also concluded that the standard American diet is undesirably and unnecessarily high in cholesterol and saturated fatty acids (a precursor of cholesterol) and that the level of blood cholesterol could be favorably altered by dietary modifications and/or specific drug therapy. They recommended that an active effort be made to reduce abnormally elevated blood cholesterol levels.

The general public is rapidly learning about the conclusions of the NHLBI Consensus Conference Report and the importance of blood cholesterol in relation to coronary artery and other vascular diseases. Furthermore, they are realizing that individuals can favorably modify their susceptibility to these diseases by lowering their blood cholesterol levels. This awareness has increased the demand for cholesterol testing. The increased demand has been further stimulated by the development of a new type of instrument for determining cholesterol levels. These new instruments determine the blood cholesterol within minutes, from only a drop of blood obtained from a "fingerstick". More conventional determinations of cholesterol require 5 to 10 ml of blood obtained from a vein and several relatively complex and time-consuming analytic procedures.

Instruments analyzing "fingerstick" samples can be operated by persons with less training than that required to operate the instruments used to analyze larger blood samples. However, there is widespread concern among the scientific community that the easy-to-operate "fingerstick" type of instruments may not always give accurate reproducible results, especially when operated by persons with little or no laboratory training and experience.

The public's desire to know their cholesterol value and the simplification of the cholesterol measuring techniques has lead to widespread testing in some areas of the United States. This enthusiasm to be tested for cholesterol on the part of the public and to test for cholesterol on the part of the civic minded and/or entrepreneurially motivated individuals is reminiscent of the enthusiasm associated with screening the public to identify individuals with an elevated blood pressure a decade or more ago.

Experience with such blood pressure screenings demonstrated that unless great care is taken in training and supervising the screeners, inaccurate blood pressure measurements were frequently reported to individuals. A single blood pressure measurement reported to an individual without appropriate advice and intelligent counseling as to the significance frequently did the individual a disservice and unnecessarily burdened the health care delivery system. Similar concerns apply to cholesterol screening.

Some of the public screenings for cholesterol utilizing the newly developed "fingerstick" instruments have been and continue to be performed by persons without the proper laboratory and counseling training. In some cases these individuals are functioning with little or no supervision. There is also fear that some screeners have had little or no training regarding infection control measures to prevent the transmission of human immunodeficiency virus (HIV), which causes acquired immunodeficiency syndrome (AIDS); and other diseases such as hepatitis B. The potential for such disease transmission to occur is especially great when screening is carried out in public places such as shopping malls, parking lots and retail stores where qualified laboratory supervision would not be available without careful planning.

It should also be noted that with the evolution of technology permitting blood cholesterol levels to be determined on a drop of blood, that similar technology will be available to permit determining a whole host of other blood components.

The purpose of this Report is to discuss the desirability and feasibility of providing the citizens of Florida with more widespread access to accurately determined and appropriately reported cholesterol tests.

SHOULD CHOLESTEROL SCREENING BE MADE MORE READILY AVAILABLE TO THE PUBLIC?

As emphasized in the introduction, public demand for cholesterol testing is increasing. This demand has already caused some poorly-trained and inadequately-supervised persons to offer testing to the public in Florida. As the number of persons offering cholesterol testing increases, it will become more difficult to regulate the quality of such testing.

In view of this high demand for cholesterol screening/ education and the potential for improving the health of the citizens of the state, it should be made more readily available to the extent that it can be done accurately. Screening should not be done if it cannot be done in accordance with currently accepted laboratory standards for precision, accuracy and in accordance with nationally accepted guidelines.

Some of the portable cholesterol measuring instruments have been shown to be of acceptable accuracy and precision most of the time if used by properly trained persons. Our challenge is to ensure that only properly trained persons perform these tests using reliable instrumentation and quality assurance guidelines.

Wherever cholesterol screening is performed, an accurate number is only the beginning. A person must know what action to take as a result of that number, what dietary changes should be made and whether a physician should be consulted. These questions must be addressed whenever cholesterol testing is performed.

In addition to asking how "cholesterol testing can be properly expanded, concern must be given to how this expanded testing can be targeted to reach those groups needing it most. Minority groups can be significantly under-represented if screening occurs only in certain locations. Attempts should be made to perform screening at multiple sites within a community so that the screened population represents the entire community, including high-risk groups.

STANDARDS FOR CHOLESTEROL TESTING

RECRUITMENT:

As recommended by NHLBI, recruitment strategies should be constructed to take account of the following needs:

- o Marketing approaches that emphasize participation of the entire adult population.
- o Targeted screening at sites where underserved populations are found.
- o Flexible hours at the screening site, including evenings and weekends, for maximum availability.
- o Screening facilities that are accessible and affordable to all elements of the population.
- o Recruitment of individuals unaware of their cholesterol level, to enhance detection of new high-risk cases and to discourage substitution of screening for medical care.

INSTRUMENTATION:

Instruments should meet the performance standards established by the Laboratory Standardization Panel of the National Cholesterol Education Program (NCEP), having precision and accuracy of within 5% (3% by 1992). The analytical aspects of the screening program should be supervised by a responsible representative of a licensed clinical chemistry laboratory. This laboratory must be used for consultation for the technical aspects of cholesterol measurements.

All analyzers should undergo a prefield evaluation in a licensed clinical chemistry laboratory, to document acceptable performance. At least two control samples, traceable to the National Reference System for Cholesterol Measurements, established by the Centers for Disease Control and the National Institute of Standards and Technology, with values near the cut-off points established by the NCEP Adult Treatment Panel (200 mg/dl and 240 mg/dl), should be assayed in the laboratory over a two-week period on a minimum of ten different days. The results should be evaluated using appropriate statistical measures such as standard deviation (SD) and coefficient of variation (CV) to determine congruence with NCEP guidelines.

If several instruments are to be used, between instrument variability should be established by running duplicate samples on each instrument over a similar time period, and calculating inter-analyzer precision.

Prefield evaluation should also include verification of linearity, method validation, correlation studies between the instrument and the reference (consulting) laboratory and the evaluation of random errors* and systematic errors** inherent in the test system.

In the field, instruments should be calibrated daily before use; analytic instruments tend to lose calibration upon moving and storage. Each instrument should be identified (ID #) and have an operating manual containing the following:

- o Standard Operating Procedure (according to the National Committee for Clinical Laboratory Standards # GP2-A).
- o Daily check lists of critical operating characteristics (signed by operator and supervisor).
- o Record of daily calibration and quality control, signed by operator and supervisor.
- o Daily record of reagent and control lot numbers and expiration date.
- o Results of prefield testing.
- o Corrective action documentation and outcomes.
- o Preventative maintenance schedule and log.

*Random error - a variation whose source cannot be completely identified and controlled, an error due to chance.

**Systematic error - an error that occurs within the methodology or instrumentation, i.e., an inherent error; errors due to factors other than chance.

The daily check list of critical operating characteristics should be monitored prior to start-up. Daily and periodic maintenance should be completed and documented in the manual. All daily checks should be reviewed and signed by the supervisor.

QUALITY CONTROL:

There should be written quality control policies and procedures to include expected outcomes for internal and external quality control. Once an instrument is determined to meet standards of operation in prefield testing, it should be subject to continuing quality control procedures to document and monitor good performance of the test system (analyzer, reagents, and operator) and provide statistical validity and reliability of the results. Accuracy* and precision** of cholesterol assays is critical for the classification and referral of screening participants. Documented evidence of the quality control should be evaluated at least weekly by a licensed technologist and monthly by a licensed director. All corrective actions taken for measurements outside accepted ranges must be documented.

*agreement with the true value.

*Accuracy - the degree to which a measure reflects the true value.

**Precision - reproducibility.

INTERNAL QUALITY CONTROL:

Internal quality control monitors the precision of the test system (random error). This includes the assay and evaluation of several known control samples at various values and the monitoring of reagents, controls, and standards for lot number, expiration date and proper labeling.

At least two control samples should be run at the beginning of each day, after calibration of the analyzer. These control samples should be traceable to the National Reference System for Cholesterol Measurements, and should be previously assayed to determine statistically significant limits of precision (± 2 SD). Two control samples should also be run after every 20 patients and at the end of the day. All control values should be documented. A mean value and standard deviation should be established for controls. When control measurements fall outside established limits they should be remeasured. If controls run on that instrument are still outside of these limits it should not be used again until the problem is investigated and remedial action taken and documented.

The standard deviation and coefficient of variation should be calculated using that week's quality control results to foresee a trend or shift in the mean. Slight changes in the operating system *may not be detected by daily quality control evaluation.* The week-to-week analysis may identify systematic errors that can lead to imprecise or inaccurate measurements. The values obtained should be documented and reviewed by the laboratory supervisor.

EXTERNAL QUALITY CONTROL:

External quality control evaluates accuracy. This type of quality control involves comparative analysis of "blind" samples with reference and peer group laboratories using similar instrumentation and methodology.

SUPERVISION:

A state-licensed Clinical Laboratory Director or Supervisor, licensed in chemistry, should supervise the technical aspects of cholesterol measurement and delegate responsibilities as appropriate. Overall supervision may be performed by anyone knowledgeable of the standards for cholesterol screening and skilled in general administration.

PERSONNEL:

General training for all cholesterol screening program staff must include the following:

- o Importance of professional appearance and conduct.
- o Understanding of the confidential nature of personal health information.
- o All screening personnel should have clear and visible identification badges.
- o Ability to deal with emergency situations such as fainting, anxiety reactions and others.
- o Understanding the importance of accurate reporting of information and documentation of screenings, referrals and follow-up.

It is recommended that persons performing any portion of a cholesterol screening be trained in each component so they can adequately answer participant questions. In addition, those persons meeting the qualifications could be cross trained to perform any part of the cholesterol screening.

Blood Collectors -

Because errors in measurement frequently originate in poor sampling methods, persons who collect blood should be properly trained. They should have a clear understanding of sample collection methodology, and how poor technique could affect cholesterol values.

Persons who collect blood must also understand safe techniques for infection control and prevention. This should include education on the Center for Disease Control recommendations for preventing the transmission of human immunodeficiency virus (HIV) or hepatitis B in health care settings.

Persons who collect blood should be specifically trained in dealing with participants who faint, bleed excessively or develop other medical emergencies common to screening activities.

Training should include a one-week period of supervised blood collection.

Qualifications -

Blood drawers should have successfully completed the required training program and have one or more of the following minimum qualifications: a) a science degree (A.S., B.S., M.S., etc.); b) be a licensed nurse; c) be a phlebotomist; or d) be directly supervised by an individual classified in either a) or b) above.

Instrument Operators -

It is recommended that screening programs use state licensed clinical laboratory professionals to operate screening instruments.

If non-laboratory personnel are used to perform screening the time required to train them will depend upon their education and background. They should be able to demonstrate, to the satisfaction of the laboratory supervisor, competence in instrument calibration, routine operation, quality control, problem detection and routine maintenance. They should also receive a week of closely-supervised field experience before operating an instrument in the field. A clinical laboratory license and/or documentation of training should be maintained on-site.

Qualifications -

Instrument operators should have successfully completed the required training program and have one or more of the following minimum qualifications: a) a science degree (A.S., B.S., M.S., etc.); b) be a licensed nurse; c) be directly supervised by an individual classified in either a) or b) above; or d) persons having at least thirty (30) hours of documented directly supervised field experience operating the instrument for cholesterol analysis before operating the instrument alone, under the general supervision of an individual classified in either a) or b) above.

Educators/Counselors -

Persons who provide information to participants should receive training in the delivery of accurate educational messages. This should include teaching skills for clear, credible, and persuasive educational counseling and referral according to the National Cholesterol Education Program guidelines. In addition, training should include information on the various community resources for health care including hospitals, clinics and public health agencies. It is recognized that in-depth counseling cannot be expected in the screening setting; however, a simplified, clear message should be provided as well as factual answers to questions. The amount of training required to achieve this standard will depend upon an individual background. It can be anticipated that for persons with a health care background (e.g., registered nurse) this training can be expected to take about eight hours.

Qualifications -

Persons providing information and referral to participants should have successfully completed the required training program and have one or more of the following minimum qualifications: a) a science degree (A.S., B.S., M.S., etc.); b) be a licensed nurse; or c) be directly supervised by an individual classified in either a) or b) above.

It is possible that one person could collect the blood sample, operate the instrument and educate/counsel a screenee. Obviously that person must be trained in each of these aspects of cholesterol screening, and have enough time to perform each step in accordance with these standards.

RECORDS AND RESULTS:

The screening staff should maintain logs of all participants, their results, and the instrument utilized. Records on each participant should include their name, address and telephone number (needed for follow-up), the identity of the blood collector, analyzer operator, and date and time of testing. The instrument should ideally provide a "hard-copy" of the results to minimize transcription errors and maximize participants' privacy in receiving their values.

Preventative maintenance and associated instrument records should be maintained with the instrument as long as it is in operation. The records and logs of participants should be maintained for at least two years, including quality control and proficiency testing results. The license or training documentation of blood collectors and instrument operators should be kept on-site.

BIOHAZARDOUS WASTE/INFECTION CONTROL:

All sharp or jagged objects, including but not limited to capillary tubes, needles or lancets, should be placed in a rigid disposable container labeled "BIOHAZARD" and indicate the identity of the screening facility. All potentially infectious materials should be disposed of according to current State and Federal guidelines.

All staff must have documented training in infection control procedures. Gloves, disinfectants, plastic aprons and other safety devices should be available for use. A sink for handwashing or other appropriate method for disinfection must be located at the screening site in order to prevent transmission of disease.

FACILITIES:

There should be a general manual of operations that includes all procedures within the screening center and lists minimal space requirements. Most health care screening activities occur in malls, department stores, etc. (i.e., non-medical facilities); guidelines for site selection should be considered. Screening programs should make provision for the following environmental considerations:

- o The facility should be conducive to handling the flow of participants.
- o Confidentiality and privacy should be assured during cholesterol screening.
- o There should be adequate staff to handle anticipated numbers of participants; a stressful, cramped, hurried environment may lead to low quality results and an increased likelihood of errors.
- o There should be adequate lighting and location of essential utilities.
- o There must be appropriate facilities for disinfection at the screening site, e.g., a sink or suitable chemicals which may be applied to the skin for disinfection.
- o Room temperature must be maintained within the analyzers' specifications.

COUNSELING AND REFERRAL STANDARDS:

Any cholesterol screening program designed to increase public awareness of cholesterol and its relation to coronary heart disease (CHD) must include counseling and referral components. These two areas are the weakest part of current cholesterol screening programs. Educational materials should be included as part of any screening with knowledgeable staff providing accurate written and verbal information.

Education programs need to identify special high-risk groups and develop recruitment approaches to attract these designated target groups. Persons doing screening should have access to appropriate health care professionals for consultation. Also, currently available community health care resources need to be incorporated into public screenings. Active referral and follow-up programs need to be instituted to increase the number of referred screenees who reach medical care. Letters or phone calls may be needed to assure proper follow-up. Finally, education programs need to raise public consciousness and knowledge about coronary heart disease and cholesterol.

Prior to initiating a referral system for persons with elevated cholesterol, one must assess the readiness of the health care system to receive referrals. Questions which must be answered include: Are physicians willing to accept the potentially large number of clients for medical care, dietary prescriptions and counseling? Are physicians willing to treat and at what levels? Are dietary and nutrition counseling services available? Who will assume the costs of referral and follow-up?

Assuming the capability of accurate testing and health care provider readiness, at a minimum, counseling and referral should include the following standards:

- o Immediate on-site, individualized counseling and education appropriate to the results is necessary.
- o Counseling and education requires professional judgement that uses the actual cholesterol test number and the evaluation of the presence of other risk factors as a basis for action. This includes reinforcement of positive practices and lifestyles for clients with "good" results and appropriate referral for less desirable results.
- o The counseling and education provided should include information on cholesterol and coronary heart disease and should be provided with the cholesterol measurements. This can improve knowledge, attitudes and health behaviors.
- o Printed, verbal and video educational messages can all be used to convey messages in a clear and understandable format.
- o The needs of minorities, special ethnic groups and participants with unique cultural backgrounds should also be accommodated.
- o Referrals should address the importance of physician follow-up, the need for additional cholesterol testing and where additional services may be obtained.

- o Active follow-up programs are the responsibility of the screening agency or program and are necessary to increase the likelihood that those referred reach medical care.
- o Follow-up may include telephone calls, postcards or letters within an appropriate time frame based on the individuals results. In most instances this would be within two months of the initial screening/referral date.
- o All referrals should be based on the most current accepted guidelines for the National Cholesterol Education Program (NCEP) and the American Heart Association (AHA) combined with self-reported risk factors.

The following referral criteria are currently recommended by the NCEP and the AHA and should be used:

- o Greater than or equal to 240 mg/dl - refer to medical care within two months for further follow-up.
- o 200-239 mg/dl - additional information should be sought to determine the presence of cardiovascular disease or risk factors as indicated by the NCEP.
- o If a history of cardiovascular disease or two or more risk factors are present - refer to medical care within two months.
- o If no history of cardiovascular disease or less than two risk factors - refer to medical care within one year and recommend an eating plan to reduce high blood cholesterol levels.
- o Less than 200 mg/dl - advise participant concerning healthy eating patterns, the importance of regular checks of cholesterol (every 5 years) and the fact that cholesterol screening is not a substitute for regular medical care.
- o A screening program must have liaisons with local resources such as hospitals, clinics, the medical community and public health agencies in order to refer clients to a local facility within his/her geographic area and economic capability.
- o The screening program should maintain current written/printed lists of community resources including addresses, telephone numbers, fees and a description of services which can be given to those participants with abnormal results or those requesting such information.

- o Follow-up procedures must be carefully planned before implementing a cholesterol screening program, including a training procedure which specifies how follow-up will be carried out, (e.g., phone or mail), what message will be given and what information will be collected; follow-up procedures generally use a minimum of three valid attempts of contact prior to closing a file.

In summary, education, counseling, referral and follow-up are all critical elements of cholesterol screening. A screening program which is deficient in these elements may not be effective, does not meet recognized standards and may be a disservice to those participating in the program.

CONCLUSION

In closing, testing for cholesterol is a complex issue. It is critical that accurate and safe testing be provided to Floridians. Those testing should adhere to standard protocols and the recommendations of the National Cholesterol Education Program and the American Heart Association. Proficiency requirements must be met in all aspects of testing and measures to insure compliance and regulation of minimum standards should be incorporated into current laboratory regulations.



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
8757 Georgia Avenue
Silver Spring MD 20910

FEB 3 1989

Laura M. Phillips, M.A.
Biological Administrator
Laboratory Licensure Section
State of Florida
Department of Health Rehabilitative Services
2727 Mahan Drive
Tallahassee, Florida 32308

RECEIVED LEGAL

FEB 23 1989

HRS Office of Licensure
and Certification

OFFICE OF LICENSURE
RECEIVED
FEB 23 1989
AND CERTIFICATION

Dear Ms. Phillips:

This is in reply to your letter of January 13th requesting information on the marketing clearance by FDA of four specific devices presently in commercial distribution in your state. Based on our records the following determinations have been made on these devices.

1. The KDI Quick Test, manufactured by Keystone Diagnostics. Our records show that marketing clearance under the Premarket Notification Procedures (21 CFR section 807.87), was given to the KDI Quick Test Drug Screen on March 3, 1986 for professional use in forensic toxicology laboratories for screening, by qualitative detection of abused substances, to determine the need for additional or confirmatory testing.
2. LipoScreen TC - manufactured by Home Diagnostics, Inc. for cholesterol tests. No clearance was given to a product by this name. Our records show that clearance was given to another company, Technimed Corporation, Fort Lauderdale, Florida, for the marketing of a reagent strip for the semi-quantitative determination of cholesterol in whole blood. The manufacturer utilized the data collected in Home Diagnostics Laboratory for the evaluation of its product. That device, Dimension Whole Blood Cholesterol Strips, was cleared for marketing on November 8, 1988 for professional use in physician office laboratories, for screening to identify elevated blood cholesterol levels.
3. Chemcard - manufactured by Chematics, Inc. No clearance was given to a product by this name. Our records show that marketing clearance was given to another product "Solid Phase Determination of Serum Cholesterol from Whole Blood", subsequently called with a similar name, Clinicard® Cholesterol, by Chem-Elec, Inc.; North Webster, Indiana. It is a test for the semi-quantitative determination of cholesterol in whole blood. That device was cleared for marketing on June 10, 1988 for professional use in physician office laboratories, for screening to identify elevated blood cholesterol levels.

Page 2 - Laura M. Phillips, M.A.

4. The Reflotron - manufactured by Boehringer Mannheim Diagnostics. Our records show that this device was cleared for professional use in physician office laboratories on September 16, 1985. Because whole blood may be used with the dry strip technology utilized in the Reflotron, selected users may have used the device in cholesterol screening in locations other than physician office laboratories. However, the device was not cleared to be sold to "anyone". The System is used with a variety of specimens (venous serum or plasma) which are analyzed in a professional setting.

None of the above devices were cleared for home use or for direct sale to nonprofessional consumers.

Please refer to the package inserts of the devices for information on accuracy.

Sincerely yours,

Jerome A. Donlon, M.D., Ph.D.

Jerome A. Donlon, M.D., Ph.D.
Division of Clinical Laboratory Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Cholesterol tests: Hot number, or wrong number?

FBy Susan Hall
run Wheeler tells of one
of her nurses who, after
two days of special
training, tested nearly 100
people in a cholesterol screen-
ing before realizing she had
been inserting the blood sam-
ple into a cholesterol ana-
lyzer upside down.

The instrument will give
you a number—in this case,
they all ranged between 211
and 216," Wheeler said. "But in
the haste and bustle of screen-
ing a lot of people, it took her a
long time to see that something
was going on."

"Luckily, it happened during
a practice screening of health
department personnel. But it
shows you that there are an un-
usually number of ways to do it
wrong," asked Wheeler, who is
director of the South Carolina
Department of Health's Center
for Health Promotion.

Cholesterol screening is a
"hot button" all across the
country. And who's got the
last word? Drug stores, eager to
sharpen their health care im-
age and pull traffic, supermar-
kets, cashing in on the public's
growing appetite for low cho-
lesterol foods, a growing num-
ber of corporations and other
workplaces, malls, state fair-
grounds, even flea markets.

Finled by concerted efforts
of the nation's health care insti-
tutions to raise public aware-
ness of cholesterol and its re-
lationship to heart disease,
"Know Your Number" has be-
come the battle cry of the hour.
But there's one way to show
that the caliber of public blood
cholesterol screenings is no
even as to render that number
questionable, if not mean-
ingless, in many cases.

• Screening often don't know
how to perform a good finger-
stick properly, much less carry
out quality control procedures.
• As much as 30 percent of pa-
tients in a screening can be
misclassified.
• Doctors and other local
health professionals aren't
getting the advance notice
they need to prepare for the
increased case load a screen-
ing can generate.

• Some customers are being
given their cholesterol num-
ber with little or no education
or counseling on what that
number means.

• There is often no referral or
follow-up of high-risk patients.

• In most states, public
screenings are unregulated.
If drug stores who offer cho-
lesterol screenings want to
maintain credibility with cus-
tomers, health care experts
warn, they must make sure
those cholesterol numbers are
as accurate and meaningful as
possible. And that means
screening the screener they
plan to use with utmost care.

"People think, 'It's only a
screening,' so as to suggest ac-
curacy isn't all that important
because inaccurate results
won't harm people," said Dr.
Sain Thompson, director of
New Jersey's Clinical Labo-
ratory Improvement Service.
"But what's the use of testing if
half the results are wrong? True,
false positive poses no
harm, except possibly psycho-
logical. But a false negative
could be harmful."

Screening chains up fourfold: survey

Drug Store News conducted a survey on
what the top 100 chains are doing in the area
of health care screenings. (Thirty-eight
chains had responded to the survey at press
time.) The complete survey results are sched-
uled to appear in the next issue. Here are
highlights of our findings:

• Four times as many chains who respon-
ded are offering cholesterol screenings now
than two years ago (29 in 1989, 8 in 1987).

• The average customer participation per
day in a store for a cholesterol screening is 111
people, much more traffic than for any of the
other six types of screenings surveyed.

• Half the respondents ranked contribution
to their health care image as the primary rea-

son for offering cholesterol and other screen-
ings. Building traffic was second most fre-
quently cited as top factor.

• Almost half (16) of the respondents said
they offer cholesterol screenings four or more
times a year. Eleven offer them once or twice
a year and two less frequently.

• More than half the respondents (23) said
they collaborate with an outside group to of-
fer cholesterol screenings, with 18 indicating
they use a "turnkey" company.

• Most chains charge a fee for screenings, the
average being \$6.28. But of the 27 respon-
dents who charge, 23 said the fee is to cover
costs, and 4 said they expect to make a profit
from the fee.

A team led by Dr. Russell
Loepker, professor of epi-
demiology and medicine at the
University of Minnesota, re-
cently monitored several cho-
lesterol screening programs
run by commercial concerns
and others, and found a wide
variation in the quality of their
cholesterol measurements.

"Even the best-run pro-

gram, using the most expen-
sive machines, misclassify
(patients) at the 10 percent
level," Dr. Loepker found.
"When done badly, misclas-
sification is at 30 percent."

In the past few years, tech-
nological advances have pro-
duced cholesterol screening
instruments—such as Hoch-
ranger Mannheim's Reflotron,
Eastman Kodak's DT-60 and

use, touching off an explosion
of public cholesterol screen-
ings and opening up a market
that, according to the three
major manufacturers of the in-
struments, is in the millions of
dollars, and growing.

The instruments themselves
are monitored by the Centers
for Disease Control (CDC).

Dr. Herbert Naito, a clinical
biochemist with the Cleveland

a system that is less depen-
dent on the operator's skill.

"People running a screening
program must follow quality
control and quality assurance
procedures," he explained.
"But many people without a
laboratory background don't
know how to do quality control
properly, so it's a junk in to
have an outside clinical chemist
or certified medical technol-
ogist audit the program."

Dr. Naito's group also eval-
uated the Chemcard, a whole
blood, non-instrument test for
cholesterol marketed by Che-
mules of North Webster, Ind.,
and approved for profes-
sional use in September by the
Food and Drug Administra-
tion. According to Dr. Naito,
"Even in experienced hands,
it's very difficult to get valid
results. It gives very broad
ranges. Just getting ranges
left the way to go."

He said the FDA needs to
tighten its criteria for approval
of such devices.

"If a cholesterol reading is
high or low, it's a loose-lace
situation for the consumer," said
Keith Schucker, research ad-
ministrator at the National
Heart, Lung and Blood In-
stitute (NHLBI), which recently
issued recommendations on
public cholesterol screenings.
"Although our research shows
that people don't go out and
binge on the basis of a low
reading, if they get a high
reading, they're out the cost of
a doctor's office visit and of an-
other lab test (to verify the
first result)."

All sorts of factors can affect
cholesterol measurement,
health care sources point out.
For example, a cholesterol
reading will be 5 percent higher
if the patient is standing
rather than sitting.

In addition, the fingerstick
procedure can show results un-
der several conditions, includ-
ing if the finger is "milky"
(massaged or squeezed) after
the puncture, causing dilution
of the sample. Yet the finger-
stick is often perceived as re-
quiring no special skill. The
makers of Chemcard, for exam-

Continued on page 1113



Customers have their cholesterol checked for a \$7 fee at a screening at a Pharm-Blue store in Orlando, Fla. The state recently brought an injunction against Heart Check, the "turnkey" cholesterol screening company doing the screening in the above photo, claiming it is unlicensed and in violation of the state's clinical lab law. The two-day screening drew 200 to 300 customers a day, said David Catala, central Florida Heart Check affiliate.

What to look for in a screener:

1. What are the qualifications and reputation of the people who will do the screening for you?
2. Has the screening organization complied with state regulations?
3. What are the screener's procedures for continuous quality control and quality assurance of instruments and testing?
4. Will a written informed consent form be used?
5. Who is the screening coordinator and will that person be readily available in case a problem arises during the screening?

6. What is the extent of on-site counseling provided by the screener?
7. Will contacts be made with the local medical community well ahead of the screening day to alert physicians and other health care professionals of the screening? What provision has been made for physician referral of abnormal results?
8. Does the screening group have follow-up strategies for high-risk patients?
9. How will medical waste be disposed of?
10. Does the screening agency carry professional liability insurance?

cholesterol screening controversy

Continued from page 1711
 ple, especially heard from a Midwestern pharmacist who said that in his state, he was prohibited from performing a fingerstick triglyceride test. His solution was to have his customers prick their own fingers.

In addition, Dr. Gerald H. Cooper, research medical officer with the FDA, points out that people can vary by 10 to 15 percent from day to day and work to work in their readings.

"We must get across that one measurement is not holy. It takes the average of two or three measurements over time to know an individual's true cholesterol measurement."

With consumers growing clamor to know their number has come a proliferation of cholesterol screening eager to meet that demand. "I can't recall any other time when so many people have jumped in to make a buck—some are well qualified, and some know nothing," said New Jersey's Dr. Thompson.

Cholesterol screenings are not only lucrative for the for-profit "turnkey" screening companies, which charge from \$5 to \$14 per test, but have become an effective means of generating wheel sales for drug stores, supermarket health centers, through promotions such as coupons and in-store displays of low-cholesterol products. In addition, food companies such as Kellogg are hyping low cholesterol and cholesterol-free products.

Nothing health care professionals and commercial cholesterol screening agree on is that training is crucial to a good cholesterol screening program.

One commercial screener recalls watching drug store employees unplug an instrument from a crate: "They had the manual out, but it took them 20 minutes just to figure out how to turn the thing on," he said. He said he had also seen screeners "dump lanes in ordinary wastebaskets."

Some screening companies train their own personnel. Heart Check, for example, which does not require hirees to have a medical or scientific background, offers an in-house certification program.

However, some screening entrepreneurs are so busy processing people's numbers to make a profit that they're not careful procedures and personnel training," said Jerry Wilson of Citizens for Public Action on Cholesterol. "But that's not unique to them. We've found professionals who don't know how to calibrate or stick fingers properly."

Although some health care professionals grant that any individual performing an in-home test must be properly trained and supervised, be a competent cholesterol screen-

er, must prefer medical technology or others with a medical background as screeners. They point out that, in addition to technical knowledge, they are more qualified to provide competent counseling and education.

Indeed, some screeners provide only the screener's number and brochure, to avail a list of physicians.

From Wheeler says if she

sees an advertisement for a screening in a drug store or mail, she checks it out. "In one drug store, I found one RN—none of the rest were lab technicians or RNs; they were just following manufacturer guidelines. After I received my cholesterol number, I asked, 'What do I do now?' The screener didn't know what the number meant. I was just told to go to my doctor."

Some commercial screening companies invest heavily in

professional and general liability insurance, covering both the company and individual screeners, even though it represents a major expense.

In addition to carrying liability insurance, "The labs are changed every time, our technicians wear disposable gloves and we use standard sterile techniques," said Jerry Barth, a pharmacist who runs Gold Medical Screening, based in Mankato, Minn., with his wife, Diana, a coronary care nurse.

"That's about all we can do at this point, except we have the patients sign a form, releasing the company and retailer from liability."

"It's come out there in most states," said Dr. Gary Myers, the Centers for Disease Control's chief of Clinical Chemical Standards Activities, of public cholesterol screenings. "The best the states can do is try to control it and educate people doing the screenings to do a proper job."



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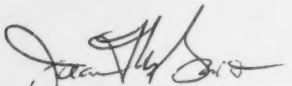
May 1, 1989

Representative Ron Wyden
Chairman
Committee on Small Business
Subcommittee on Regulation,
Business Opportunities, and Energy
B-363 Rayburn House Office Bldg.
Washington, DC 20515

Dear Congressman Wyden,

I regret that other commitments prevented me from submitting these responses sooner. I hope the following comments will be helpful in your final assessment of the hearing. Please let me know if you have any further questions.

Sincerely,



Jean Flatley McGuire
Executive Director

Answers to Questions Posed Regarding
HIV Home Test Kit Testimony (March 23, 1989)

1. Particularly as the demographics of the epidemic shift, individuals coming in to ascertain their HIV status are increasingly likely to be less familiar with preventive care options and less equipped to deal with negotiating the difficulties of accessing our public health structures. The post-test counseling session provides an important opportunity to establish the linkages that will be necessary to help the person maintain their health status as long as possible. In some settings that means direct assistance in applying for Medicaid and SSI; in others it means actually setting up the primary care appointments that should follow. This linkage becomes increasingly important as we find new interventions that will truly result in prolonging life and in keeping people out of more expensive and less restrictive care settings.

2. Much of the HIV prevention education and counseling is already being provided outside of traditional medical settings, since most of the alternative test sites are located in non-medical community based settings. What is important is that the opportunity be provided for the education and counseling in as intimate and culturally appropriate setting as possible. In addition, we continue to need to develop further capacity to extend the support offered in the post-test counseling process so that people will continue to have access to the assistance they need to maintain behavior change - but that first linkage for achieving behavior change comes through the initial post-test counseling process. The potential for achieving change will frequently be only as good or bad as the post test interaction.

3. One would certainly be the lack of the linkage to the services we have already discussed. Beyond that would be the considerable concerns about how the individual would psychologically handle the impact of the information, particularly if they are in a setting already lacking in support structures. Without feeling the linkage to a system that would potentially offer them assistance with which to cope with the disease, the potential for life-threatening behavior could increase.

4. This question, as well as the one above, is probably better put to a person with counseling and support experience with the minority population. As our testimony noted there is no concrete research which would lead us to believe that phone counseling would be efficacious. Furthermore, there is the very practical reality that for any population there is nothing to keep the person from simply hanging up the phone at any point in the conversation.

5. The availability of a home test kit is very likely to significantly increase the numbers of people getting tested,

particularly those who constitute the "worried well." We are far more concerned about the potential of rising false positives than we are about the possibility of increased need for additional counseling support. Frankly, as we find more promising interventions and encourage more people to get tested, there will be a considerable increase, not only for pre- and post- test counseling support, but also for long term assistance.

6. The first and most important change that must be realized is for the enactment of broad based anti-discrimination protections as envisioned in the Americans with Disabilities Act. Beyond that, there is a great need to roll back those restrictive reporting measures that have emerged in some states and assess alternatives for dealing with the grave impact a positive test can have on one's ability to get or sustain health insurance.

7. I have referred this question to the American Psychological Association.

8. See # 4

9. No. Although I am not a clinician, you have certainly heard from a number who present what I think are compelling arguments regarding the need for visual interaction to assess a person's mental health status. Certainly, that was true in my many years of running residential settings for severely disabled individuals; I cannot imagine it is any less true in this context.

10. To the best of my knowledge, there is no issue that parallels HIV for which phone counseling is currently undertaken. Furthermore, because of the life and death nature of the information that an individual would be receiving, I cannot imagine suggesting a parallel with other telephone interventions.

11. The federal government should be at the forefront of increasing the numbers of HIV anonymous testing sites. As you know, the NORA coalition has suggested a considerable increase above the President's budget for precisely this purpose. Broader availability of alternative testing sites would accommodate what we expect to be the increasing numbers of persons seeking HIV testing as new interventions become available. Whether or not such availability will negate the need for home test kits depends on whether or not you believe there exists such a need to begin with. I don't, and at this point neither does most of the public health community.

12. This is truly one of the circular arguments in the promotion of the home test kit. If the reason for testing at home is one's fear of the current health system, then there is no reason to assume that a private in home test is going to do anything to reduce that fear for the person who may be positive and is going to need those linkages more than ever. The only thing that will reduce the fear associated with testing is to remove the fear of discrimination and the fear of loss of health care coverage.

**FEDERAL EXPRESS AND FACSIMILE**

March 21, 1989

Honorable Ron Wyden, Chairman
Sub Committee on Regulation,
Business Opportunities & Energy
363 Rayburn House Office Building
Washington, DC 20515

Dear Congressman Wyden:

Thank you very much for extending to me the opportunity to testify at your hearing scheduled for March 23, 1989 regarding HIV testing. Unfortunately, due to the shortness of time (I received your invitation on March 20) and a long standing prior engagement, I will be unable to appear. I hope this letter can be of assistance to you and I would, at some other time, be pleased to appear before your Committee or meet with you or your staff.

Cambridge BioScience Corporation was founded in 1981 with a primary focus on the development of diagnostics and vaccines for human and veterinary applications. Early work focused on retroviruses, including feline leukemia. In 1982 the Company's focus was broadened to include human T-Cell leukemia virus (HTLV-I). In 1982 and 1983 the Company began its work in seeking to identify the cause of AIDS, with the hope of developing products in the area.

The Company in 1985 introduced its first product, a diagnostic test for feline leukemia. In 1986 the Company introduced its first human product, a test for Rotavirus. In 1987 and 1988, we introduced three different tests for adenovirus. During this period of time work was in progress to develop a vaccine against feline leukemia and also to develop HIV-1 screening tests.

The Company's approach to developing HIV-1 screening tests was to immediately seek to create recombinant materials, rather than relying on viral lysate, as did the manufacturers of the first generation screening tests. While this approach was certain to take longer, it held out the promise of higher sensitivity and specificity than lysate tests, with safer and more economical manufacturing techniques, and reduced lot-to-lot variation. After much research, our scientists developed a recombinant protein which we call CBre3, which is comprised of two highly

Page 2
 The Honorable Ron Wyden
 March 21, 1989

immunoreactive fragments of the envelope protein of the AIDS virus. CBre3 serves as the basis for our enzyme immunoassay (EIA) which is awaiting FDA approval, and our Recombigen[®] HIV-1 LA five minute latex agglutination test which the FDA licensed in December 1988.

When performed by properly trained professionals, the latex agglutination test gives results which are at least as sensitive and specific as the existing approved EIA tests. The test can be performed without instrumentation and, for the first time, brings together the physician, the patient, and the test. This makes possible the proper handling of the three most important aspects of an AIDS screening program - confidentiality, informed consent, and counseling both before and after the administration of the test. We believe that this can afford important protection to the patient.

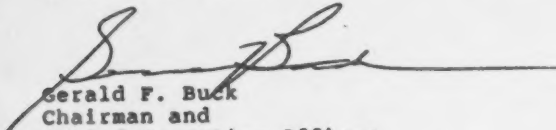
We are often asked the question, can our latex agglutination test be used as a home test? The answer is no. This test is designed for use by properly trained professionals in the health care system, and is not available for sale except to qualified health care providers. We strongly concur with the views of most commentators that proper counseling is essential to describe the limitations of the procedure, the precautions which patients should take, and to explain the results, whether positive or negative. Furthermore, because a positive result by this test should, as with all other AIDS screening tests, be re-tested by another method, the lack of ready access to such a supplementary or confirmatory test in the home is a serious drawback. Our company has been steadfast in this position for quite some time.

You have asked for information regarding our marketing arrangements with Baxter International, Inc. While the details of our arrangement are confidential, I can state that it is a relatively straightforward distribution agreement pursuant to which Baxter has the obligation, among other things, to comply with requirements established by the Food and Drug Administration. We are informed by Baxter that it is selling the latex agglutination test only to professionals in the health care system. It is of course in our interest that this be so, for it is important that the test be properly used by trained personnel; as with any test, poor technique or failure to follow the manufacturer's package insert instructions can give bad results.

Page 3
The Honorable Ron Wyden
March 21, 1989

I hope that this has been helpful to you and your committee, and I stand ready to assist you further if I can.

Very truly yours,



Gerald F. Buck
Chairman and
Chief Executive Officer

FC#6.12

MAJORITY MEMBERS
RON WYDEN, OREGON
 CHAIRMAN

ELIOT L. ENGEL, NEW YORK
 NORMAN SISKEY, VIRGINIA
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 MICHAEL R. MCWALTY, NEW YORK

101st Congress

United States House of Representatives
Committee on Small Business
Subcommittee on Regulation,
Business Opportunities, and Energy
 W-363 Rayburn House Office Building
 Washington, DC 20515

MINORITY MEMBERS
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 202-225-7727

ANDREW POWELL
 MINORITY SUBCOMMITTEE PROFESSIONAL
 STAFF MEMBER
 202-225-8139

March 24, 1989

Mr. Gerald F. Buck
 Chairman and CEO
 Cambridge BioScience Corp.
 365 Plantation Street
 Biotechnology Research Park
 Worcester, Mass. 01605

Dear Mr. Buck:

Thank you for your letter of March 21, regarding the Cambridge BioScience HIV-1 screening test.

I was sorry that neither your company, nor your marketing company -- Baxter International Inc. -- could provide corporate witnesses for our March 23 hearing regarding AIDS-HIV home testing and AIDS screening in non-traditional laboratories. However, I will keep the hearing record open for your written comments.

In those comments, I request that you specifically address your marketing program for this product.

While your kit, by all accounts, represents a significant technological advance in the science of AIDS testing, we are all aware that this is a screening device, and that a proper AIDS diagnosis requires a confirmatory test -- the Western Blot.

The Cambridge BioScience kit can be used in many more environments than earlier screening tests, and appears to be an "easier" device for test-givers than previous screening products. However, Dr. Frank Young, commissioner of the U.S. Food & Drug Administration, stated that properly trained technicians under a doctor's supervision were necessary for quality analysis of the results.

Furthermore, Dr. Donald Berns of the New York State Department of Health, testified that in the hands of the "not necessarily unsophisticated, but relatively untrained," these screening tests could produce high rates of false positive results.

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I am concerned that so-called "quick tests," despite their technical improvements, will be mis-used by the untrained, the unscrupulous and the insensitive in their efforts to make a fast profit from the exploding AIDS epidemic.

Mr. Buck, at that hearing several questions were raised regarding marketing practices for the kit. Specifically, and despite your comments that the kit "is not available for sale except to qualified health care providers," it appears that the device is being used by some customers in environments for which the test was not designed. For example, it has fallen into the hands of (1) customers who had planned to use the kit for "improper" home testing, according to regional officials of the U.S. Food & Drug Administration, and (2) a Florida screening laboratory that was recently ordered to "cease and desist" by state officials for alleged violations of state statutes.

Therefore, I would ask that you answer the following questions:

1. Does your license approval by the Food and Drug Administration include restrictions on who uses the kit and where they use it?
2. Does a detailed, written agreement exist between Baxter and Cambridge BioScience regarding the market (i.e., customers) to be pursued for sales of the kit?
3. What are the self-imposed limitations, if any, in detail, regarding who may or may not be sold the test kit?
4. What arrangements are made by Baxter or Cambridge BioScience to ensure that customers are properly trained to perform the test, and that those giving the test ensure that those tested are properly counseled regarding the meaning and accuracy of the results?
5. To what extent does Cambridge BioScience or Baxter ensure that individuals who are instructed to perform the test are "trained professionals in the health care system?" In investigating one case in Florida, subcommittee staff found that a receptionist at an AIDS screening clinic had been trained to give the test. Indeed, she demonstrated the device to my staff. The facility's director said only professional personnel administered the test and analyzed the results.
6. To what extent does Cambridge BioScience or Baxter track ultimate use of its tests? Specifically, do the companies take pains to ensure that the tests are not resold by customers to other users? Do the companies monitor to make sure that the tests are used in the environments intended in sales agreements?

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7. Does Cambridge BioScience or Baxter have data regarding the accuracy of screening kit results, in the field, to date? If so, please provide that data to the subcommittee. According to market analysts interviewed by subcommittee staff, Cambridge BioScience is working on a new edition of the kit in which physical results are color-coded. Is this an indication of unexpected difficulty in reading results in the kit version now on the market, or is it merely a further refinement of the product?

8. Some state officials interviewed by subcommittee staff voiced concern about possible "black market" domestic distribution of quick-tests kits sold overseas. Do you share this concern, and, if so, what safeguards do the companies have to prevent proliferation of kits in unlicensed U.S. markets?

Let me reiterate, Mr. Buck, that I know we share a common interest in maintaining a responsible AIDS-HIV testing environment that both protects consumers and ensures accurate test results. Subcommittee staff has indicated that your company has been most forthcoming in our investigation, and I hope that good relationship continues.

Again, thank you for your cooperation in this matter.

Sincerely,



RON WYDEN
Chairman

cc. Dr. Frank Young, USFDA
Dr. Donald Berns, NYState Health Department
Mr. Craig Rothman, Pandex Corporation



Cambridge
BioScience

EXPRESS MAIL

April 17, 1989

The Honorable Ron Wyden, Chairman
Sub-committee on Regulation,
Business Opportunities & Energy
363 Rayburn House Office Building
Washington, DC 20515

Dear Congressman Wyden:

This letter is in response to your letter March 24, 1989 requesting written comments relative to the inquiry of the Sub-committee on Regulation, Business Opportunities, and Energy. I regret that, due to short notice and unavoidable engagement, I was unable to appear at your hearing on March 23. We had expected that my written response would be made part of the record of that proceeding; attached to this letter is a copy of my March 21 letter, and I request that both this letter and the March 21 letter be made a part of the record.

Before addressing the questions raised in your March 24 letter, I wish to clarify two points.

First, the Recombigen[®] HIV-1 LA Test is not designed to be a home test, is not labeled to be a home test, and is not sold for home use. As stated in my March 21 letter, and as we have stated on numerous prior occasions, we do not believe that home testing for HIV is appropriate, and we are not developing products for that market.

Second, I would like to clarify the purpose of HIV testing. All commercially available tests are intended to detect exposure to HIV-1 through detection of HIV-1 antibodies; they are not intended to serve as the basis for diagnosis of AIDS. The Recombigen[®] HIV-1 LA Test and the enzyme immunoassay test used by blood banks for mass screening detect antibodies to HIV-1; the Western Blot used to detect antibodies is "confirmatory" only in that it confirms the accuracy of the LA or EIA result in detecting antibodies. None of the tests indicates that a patient has AIDS, as this can be diagnosed only by a physician based upon clinical symptoms.

Page 2
The Honorable Ron Wyden
April 17, 1989

With that preface, we can answer your specific questions:

(1, 2 & 3) These questions are interrelated and refer to the intended market for the test. The FDA has restricted the customer base for this product. The intended use of the test, as set forth in the package insert, is by "properly trained personnel as a screening test in hospital laboratories, medical clinics, physicians offices, and emergency care situations, and in blood banks and other settings where enzyme immunoassays are not practical or available." Thus, the test is approved for use only in healthcare settings under the control of healthcare professionals. This test is not designed for high volume use. Rather it is intended to meet the need for a rapid screen of small numbers of samples in situations where the enzyme immunoassays are not practical or available - where, for instance, time is of the essence or the necessary instrumentation is not available.

Our marketing agreement with Baxter International is a fairly typical distribution agreement, and provides that the test must be sold in accordance with FDA Licensing. These include directives, advertisement, and, of course, customers. Clearly, the intended use, and customer base for the product, as approved by the FDA, is expected to be closely adhered to. In addition, we are advised that Baxter maintains self-imposed limitations for sale of in-vitro diagnostic products, including the following:

- Baxter does not accept cash sales. Therefore, each customer is subjected to a credit check (1st time customers are even placed on a credit limit).
- Sales are prohibited to walk-in customers.
- Baxter does not permit customers to resell product and are informed of this restriction.

Finally, if there is evidence of misuse, Baxter will cease selling to that customer.

From a commercial standpoint, we believe that there is a sizable market for this test in accordance with its intended use, and it is neither in our interest nor in the public interest to encourage use other than by qualified healthcare professionals.

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The Honorable Ron Wyden
April 17, 1989

(4) This test is only to be used by "properly trained personnel." Any test can give inaccurate results if it is improperly performed, and we have taken great pains to require proper performance of this test.

The package insert states very clearly as follows:

The apparent simplicity of this test does not obviate the need for users to develop the proficiency required for accurate interpretation of results. The agglutination patterns of this test differ from those of other latex tests. Strict adherence to the testing protocol is essential.

The language of this caution was carefully selected to warn users against careless administration of the test. The test is simple to use, but we did not want its simplicity to invite carelessness. Thus, the package insert contains detailed instructions, warnings and precautions for users, and an explanation of the limitations of the procedure.

The instructions require that users of the test use the HIV-1 latex agglutination interpretation panel to familiarize themselves with the agglutination reactions. This panel contains samples which produce reactions of varied strengths to permit users to practice using the test and reading the results as well as provide them with a proficiency panel to train other technologists. In addition, each kit contains an interpretation guide, clear photographs of the appearance of reactions of various strengths. With every first time purchase, Baxter is able to identify that customer and send him a letter to insure that they are aware of the availability of several training vehicles. At the outset, each customer is encouraged to purchase the interpretation panel. Baxter also provides customers at no charge a technical support video which enables them to be trained on correct product procedure and how to interpret agglutination reactions. The video tape also includes Baxter's 800 number for technical inquiries or complaints. Cambridge BioScience also maintains a toll free number. It is the responsibility of the healthcare professionals to ensure that his or her employees are properly trained in the conduct of the test, and we and Baxter are making every effort to facilitate that training.

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The Honorable Ron Wyden
April 17, 1989

The package insert states, "A person who has antibodies to HIV-1 is presumed to be infected with the virus and appropriate confidential counseling and medical evaluation should be offered." Proper counseling is essential, and a substantial part of our opposition to home testing is based upon the lack of availability of appropriate counseling. We rely on the healthcare professionals to offer this counseling.

(5 & 6) These questions pertain to the efforts by Cambridge BioScience or Baxter to ensure proper use of the test. We and Baxter intend to sell the test only to qualified healthcare professionals and we expect these professionals to conduct themselves in accordance with the instructions contained in the package insert; we and Baxter offer the technical support described above. Licensing qualifications vary from state to state, as does the degree of regulation. We rely on licensed professionals to obey the law but we can not assure that proper customers will not improperly use our tests. For our part, we and Baxter will sell the tests only to qualified professionals and, in the event of misuse, will stop further sales to such people. The Florida situation is an excellent case of point. We are informed by Baxter that the Florida clinic misrepresented its licensing status and that, once that situation became known, further sales were suspended. Similarly, we would expect Baxter to be alert to signs of abuse, such as unexplainably high sales to small customers.

(7) Prior to FDA approval, our test was used in clinical trials for more than 12,000 specimens, including 3000 confirmed positive samples and 9,600 confirmed negative samples. These trials were conducted under a variety of conditions, both ideal and adverse. Test performance of Recombigen[®] HIV-1 LA was investigated in parallel with licensed EIA tests in clinical studies at multiple sites. Sensitivity overall was 99.4%; specificity overall was 99.5%. We are very proud of these results and believe that we have developed an excellent test.

Baxter has not received any data nor have they had any customers allude to any problems with the product in the marketplace today. As part of the post-approval marketing process, Baxter has several programs ongoing to provide comparisons of the latex test with EIA and Western blot. To date, no data has been received from these evaluations. Both Baxter and Cambridge BioScience will monitor product performance on an ongoing basis. Baxter's tracking system

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The Honorable Ron Wyden
April 17, 1989

allows for recording the lot number of each kit that is shipped to a specific customer. This information is maintained in Baxter's database should the need arise to notify customers of a particular lot number with respect to an FDA recall. Baxter and Cambridge BioScience maintain documented product complaint files in full accordance with FDA regulation.

We are of course working on different versions of HIV tests. We, like any medical products company, are always looking for different products which meet different market needs, but this should not in any way be taken as an expression of dissatisfaction with the current test. We do not comment on specific versions under development, and specifically disclaim any comment on the assertion that we are developing a color coded test.

(8) We did not experience any difficulty in avoiding a "black market" domestic distribution of our test during the approximately eight month period prior to FDA approval when our test was available overseas but not in the United States. We are not aware of a black market in other tests. Black markets typically develop when the subject product is not legally available; in the case of HIV testing, testing is now widely available. We believe that our test makes a significant contribution by making it possible for the physician, the patient, and the test to be brought together in a single setting. This allows for informed consent, confidentiality and counseling which are so important to proper HIV testing.

Under our agreement with Baxter, we have targeted the markets previously described in the package insert. We both share everyone's concern that this product be sold to the appropriate markets and utilized by responsible, trained individuals.

I hope that these responses are helpful to your inquiry. As we have said before, we stand ready to meet with you or your staff to discuss this matter further.

Sincerely,



Gerald F. Buck
Chairman &
Chief Executive Officer



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

FOOD & DRUG ADMINISTRATION
 7300 Lake Elsworth Dr., Suite 120
 Orlando, Florida 32808

REGULATORY LETTER
 88-CRL-04
 January 27, 1988

Steve G. Levy, Owner
 National AIDS Testing Hotline, Inc.
 3801 North University Drive, #507
 Sunrise, Florida 33321

Dear Mr. Levy:

During an inspection of your firm on November 12, 1987, FDA Investigator Sonia B. Anderson documented that you are engaged in the assembly and distribution of an AIDS test kit. Our investigation has determined that your product is in serious violation of the Federal Food, Drug, and Cosmetic Act (the Act) as follows:

<u>SECTION</u>	<u>BRIEF DESCRIPTION</u>
501(f)(1)(B)	The article is adulterated in that it is a class III device which, under Section 515(a), is required to have in effect an approved application for premarket approval. The device does not have such an approved application in effect and it is not exempt from section 515 under section 520(g).
502(o)	The article is misbranded in that you have failed to register with the Food and Drug Administration (FDA) as a medical device establishment in accordance with section 510(c).

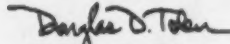
We request that you take prompt action to correct these violations. If such action is not taken, the Food and Drug Administration (FDA) is prepared to invoke regulatory actions such as seizure and/or injunction. Please advise us within ten (10) days of receipt of this letter as to the specific actions taken or intended to be taken, including measures to prevent the recurrence of the violations, and an explanation of any unforeseen delays in correcting the violations.

Information or assistance in preparing a Premarket Approval Application (PMA) for marketing of this device may be obtained by contacting Mr. Donald Hill or Ms. Mary Gustafson of the Division of Product Certification, HFN-825, Center for Biologics Evaluation and Research, 8800 Rockville Pike, Bethesda, Maryland 20892, (301) 443-5433. Registration information may be obtained from Ms. Ann E. Tornese, Device Registration and Listing Branch, H7Z-342, 8757 Georgia Avenue, Silver Spring, Maryland 20910, (301) 427-7190.

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Your response should be directed to John J. Miceli, Compliance Officer, (telephone number 305-855-0900) of our Compliance Branch at the above address. If you have any questions concerning your responsibilities or the violations listed, please contact Mr. Miceli as soon as possible.

Sincerely yours,


Douglas D. Tolen
District Director
Orlando District

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

April 26, 1988

Cory SerVaas, M.D., President
Benjamin Franklin Literary and Medical Society
1100 Waterway Boulevard
Indianapolis, IN 46202

Dear Dr. SerVaas:

During the inspection of the Saturday Evening Post Society division of the Benjamin Franklin Literary and Medical Society on December 1, 2, and 14, 1987, our investigators documented the manufacture and distribution of a blood collection kit labeled for AIDS testing. This collection kit, which includes a plastic tube for the serum sample, counseling information, directions for use, and the mailing container, is considered to be a medical device within the meaning of Section 201(h) of the Federal Food, Drug, and Cosmetic Act (FDCA Act). Because the blood collection kits were not shipped in interstate commerce for commercial distribution before the enactment of the Medical Device Amendments of May 29, 1976, such devices are automatically deemed to be class III devices within the meaning of Section 513(f) of the FDCA Act. As such, Premarket Approval (PMA) must be obtained from the Food and Drug Administration (FDA) prior to the distribution of this device to the public. Also, firms manufacturing medical devices, such as a blood collection kit intended for AIDS testing, are required to register as a medical device establishment in accordance with the FDCA Act, Section 510.

During the referenced inspection, our investigators determined that your distribution of this device has been discontinued, but that consideration is being given to begin distribution in the near future in conjunction with the Pre-Marriage License Counseling Program in Indiana. As you are aware, the FDA has the responsibility for assuring, among other things, that medical devices are effective for their intended use. While we are sympathetic to the goals of your organization in making the test available to all those who want it, it is essential that individuals be assured not only of accurate results, but also the means of understanding those results. To this end, the agency has solicited and received comments from advisory groups with knowledge of AIDS related testing issues regarding the necessary conditions and precautions required to safely market a blood

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Benjamin Franklin Literary
and Medical Society

collection kit intended for AIDS testing. The medical/scientific consensus view has been adopted by the agency and includes the following criteria which must be included in a PMA to be acceptable for filing at the present time, as follows:

1. Kits must be labeled and marketed for professional use only within a comprehensive health care environment, e.g., hospitals, medical clinics, doctor's offices, STD clinics, alternative test sites, and mental health clinics.
2. Kits must provide for the collection of a venipuncture or other appropriately validated sample by one who is recognized by a state or local authority to perform such procedures.
3. The testing sequence for all samples collected with the kits must include the use of a licensed screening test for antibody to the human immunodeficiency virus (HIV) and, for those samples testing positive by the screening test, the use of an additional more specific test, i.e., Western blot or comparable test. It is recommended that a licensed more specific test be utilized, however, the agency may accept a properly validated unlicensed test until licensed tests are more widely available.
4. The instructions for sample collection, storage, shipping, and testing must conform with or be validated as equivalent to the package insert instructions for the specific licensed HIV antibody test kit used to test samples.
5. All results of testing must be reported directly to a professional health care provider for reporting and interpretation of the result to the requestor of the test, as well as for counseling of the individual.

All collection systems for AIDS testing that meet the criteria in points 1-5 above and the requirements of 21 CFR 809.10(c) [referenced in 812.2(c)(3)] will be considered exempt from the requirement for significant risk devices of filing an application for an investigational device exemption (IDE) prior to undertaking a clinical study. Although under these circumstances an IDE application need not be filed, manufacturers should, however, follow the investigational plan outlined in 21 CFR 812.25, including the provisions for IRB approval, informed consent, and monitoring. We strongly recommend that manufacturers discuss investigational plans and clinical trial protocols with the agency prior to the initiation of investigations.

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Benjamin Franklin Literary
and Medical Society

Although the criteria outlined above represent our current approach to the regulation of these devices, we plan to seek further public comment on such issues as lay person sample collection and shipping, and counseling outside of medical settings. We will keep you apprised of matters relating to blood collection kits intended for AIDS testing, including any FDA publication of requests for written public comment or announcements of public hearings.

Further, information or assistance in preparing a PMA application may be obtained by contacting Ms. Mary Gustafson or Mr. Donald Hill of the Division of Product Certification, HFN-825, Center for Biologics Evaluation and Research, 8800 Rockville Pike, Bethesda, Maryland 20892, (301) 443-5433. Registration information may be obtained from Ms. Ann Tornese, Device Registration and Listing Branch, HF2-342, 8757 Georgia Avenue, Silver Spring, Maryland 20910, (301) 427-7100.

In view of the above, your firm should not distribute blood collection kits intended for AIDS testing until you have received approval from the FDA of a PMA application containing the requirements noted in this letter. If you have any questions or would like to meet with the agency to discuss this matter, please contact the individuals noted above or Judith A. Putz at this address.

Sincerely,

John P. Dempster
Acting District Director
Detroit District



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Services

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

REGULATORY LETTER
89-ORL-01

FOOD & DRUG ADMINISTRATION
7200 Lake Ellenor Dr., Suite 120
Orlando, Florida 32809

December 5, 1988

Edward A. Moore, President
World Wide Testing Services, Inc.
4441 N.E. 19th Terrace
Ft. Lauderdale, Florida 33308

Dear Mr. Moore:

During an inspection of your firm on July 13, 1988, Food and Drug Administration (FDA) Investigator Jeanne A. Bush documented that you are engaged in the relabeling of a Combination Blood Profile Kit (a medical device). Our investigation has determined that your product is in serious violation of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. 301, et. seq.), as follows:

SECTIONBRIEF DESCRIPTION

501(f)(1)(B)

The article is adulterated in that it is classified under Section 513(f) as a class III device which, under Section 515(a), is required to have in effect an approved application for premarket approval. The device does not have such an approved application in effect and it is not exempt from Section 515 under Section 520(g). The nature of the relabeling steps taken by you and your firm causes the device to have a new intended use that has been determined by FDA to be subject to premarket approval.

502(o)

The article is misbranded in that your firm has failed to register with FDA as a medical device establishment in accordance with Section 510(c). Your relabeling activities meet the definition of a manufacturer found at 21 CFR 807.3(d) (copy enclosed).

We request that you take prompt action to correct these deviations. If such action is not taken, the Food and Drug Administration is prepared to invoke regulatory sanctions provided under the law. These include seizure and/or injunction. Please notify this office in writing, within ten (10) days of receipt of this letter, of the specific steps you have taken to correct the noted violation.

Additionally, the agency has established specific criteria for blood collection kits labeled for HIV antibody testing and only those PMA's that meet the following criteria will be acceptable for filing:

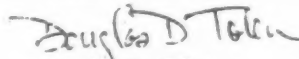
-2-

1. Kits must be labeled and marketed for professional use only within a comprehensive health care environment, e.g., hospitals, medical clinics, doctors' offices, standard clinics, alternative test sites, and mental health clinics.
2. Kits must provide for the collection of a venipuncture or other appropriately validated sample by one who is recognized by a state or local authority to perform such procedures.
3. The testing sequence for all samples collected with the kits must include use of a licensed screening test for antibody to HIV and, for those samples testing positive by the screening test, the use of an additional, more specific test, i.e., Western blot or comparable test. It is recommended that a licensed, more specific test be utilized; however, the agency may accept a properly validated unlicensed test until licensed tests are more widely available.
4. The instructions for sample collection, storage, shipping, and testing must conform with or be validated as equivalent to the package insert instructions for the specific licensed HIV antibody test kit used to test samples.
5. All results of testing must be reported directly to a professional health care provider for reporting and interpretation of the result to the requester of the test, as well as for counseling of the individual.

Information or assistance in preparing a premarket approval application (PMA) for marketing of this device may be obtained by contacting Donald Hill or Mary Gustafson of the Division of Product Certification, HFB-240, Center for Biologics Evaluation and Research, 8800 Rockville Pike, Bethesda, Maryland 20892 (telephone number 301-443-5433). Registration information may be obtained from Ann E. Tornese, Device Registration and Listing Branch, HFZ-342, 8757 Georgia Avenue, Silver Spring, Maryland 20910 (telephone number 301-427-7190).

Your response should be directed to John J. Miceli, Compliance Officer, Food and Drug Administration, 7200 Lake Ellenor Drive, Suite 120, Orlando, Florida 32809 (telephone number 305-859-8582). If you have any questions concerning your responsibilities or the violations listed, please contact Mr. Miceli as soon as possible.

Sincerely yours,



Douglas D. Tolen
District Director
Orlando District

Enclosure



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug AdministrationCERTIFIED MAIL - RETURN RECEIPT REQUESTEDREGULATORY LETTERLos Angeles District
1521 West Pico Boulevard
Los Angeles, California 90015-2486
Telephone (213) 252-7563

January 18, 1989

Mr. Palmer B. Ford, President and CEO
OMNITEC Medical Corporation
25431 Cabot Road, Suite 202
Laguna Hills, Ca 92653

LA-13-9

Dear Mr. Ford:

During inspections of OMNITEC Medical Corporation, on April 19-25, 1988 and September 9, 1988, our investigator documented that you are engaged in the assembly and distribution of a blood collection kit labeled for AIDS testing. Our investigation has determined that your product is in serious violation of the Federal Food, Drug, and Cosmetic Act as follows:

<u>SECTION</u>	<u>BRIEF DESCRIPTION</u>
501(f)(1)(B)	The article is adulterated in that it is a class III device which, under Section 515(a), is required to have in effect an approved application for premarket approval (PMA). This device does not have such an approved application in effect, and it is not exempt from Section 515 under section 520(g).
502(c)	The article is misbranded in that it is processed in an establishment not duly registered in accordance with Section 510(b) or (c), and is not included in a list as required by Section 510(j).

As you are aware, the FDA has the responsibility for assuring, among other things, that medical devices are effective for their intended use. It is essential that individuals be assured not only of accurate results, but also the means of understanding those results. To this end, the agency has solicited and received comments from advisory groups with knowledge of AIDS related testing issues regarding the necessary conditions and precautions required to safely market a blood collection kit intended for AIDS testing. The medical/scientific consensus view has been adopted by the agency and includes the following criteria which must be included in a PMA to be acceptable for filing at the present time, as follows:

Page 2 OMNITEC MED CORP (cont'd)

1. Kits must be labeled and marketed for professional use only within a comprehensive health care environment, e.g., hospitals, medical clinics, doctor's offices, STD clinics, alternative test sites, and mental health clinics.
2. Kits must provide for the collection of a venipuncture or other appropriately validated sample by one who is recognized by a state or local authority to perform such procedures.
3. The testing sequence for all samples collected with the kits must include the use of a licensed screening test for the antibody to the human immunodeficiency virus (HIV) and, for those samples testing positive by the screening test, the use of an additional, more specific test, i.e., Western blot or comparable test. It is recommended that a licensed, more specific test be utilized; however, the agency may accept a properly validated unlicensed test until licensed tests are more widely available.
4. The instructions for sample collection, storage, shipping, and testing must conform with or be validated as equivalent to the package insert instructions for the specific licensed anti-HIV test kit used to test samples.
5. All results of testing must be reported directly to a professional health care provider for reporting and interpretation of the result to the requestor of the test, as well as for counseling of the patient.

All collection systems for AIDS testing that meet the criteria in points 1-5 above and the requirements of 21 CFR 809.10(c) [referenced in 812.2(c) (3)] will be considered exempt from the requirement for significant risk devices of filing an application for an investigational device exemption (IDE) prior to undertaking a clinical study. Although under these circumstances an IDE application need not be filed, manufacturers should, however, follow the investigational plan outlined in 21 CFR 812.25, including the provisions for IRB approval, informed consent, and monitoring. We strongly recommend that sponsors discuss investigational plans and clinical trial protocols with the agency prior to the initiation of investigations.

Although the criteria outlined above represent our current approach to the regulation of these devices, we plan to seek further public comment on such issues as lay person sample collection and shipping, and counseling outside of medical settings. We will keep you apprised of matters relating to blood collection kits intended for AIDS testing, including any FDA publication of requests for written public comment or announcements of public hearings.

Page 3 OMNITEC MED CORP (cont'd)

Further, information or assistance in preparing a PMA application may be obtained by contacting Ms. Mary Gustafson or Mr. Donald Hill of the Division of Product Certification, HFB-240, Center for Biologics Evaluation and Research, 5600 Fishers Lane, Rockville, MD 20857, (301) 443-5433.

Registration information may be obtained from Ms. Ann Tornese, Device Registration and Listing Branch, HPZ-342, 8757 Georgia Avenue, Silver Spring, Maryland 20910, (301) 427-7190.

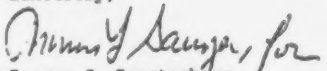
It is your responsibility to assure that each requirement of the Federal regulations is followed. We request that you take prompt action to correct the deviations. If such action is not taken, the Food and Drug Administration is prepared to invoke regulatory sanctions provided under the law. These include seizure and/or injunction.

Please notify this office in writing, within ten (10) days of receipt of this letter, of the specific steps you have taken to correct the noted violations.

Your response should be directed to:

Mr. Thomas L. Sawyer
Director, Compliance Branch
U.S. Food and Drug Administration
1521 West Pico Boulevard
Los Angeles, CA 90015

Sincerely,


George J. Gerstenberg
District Director

bcc: /HFB-100
HFA-224
HFR-PA13
HFR-PA200 (3)
HFR-PA250
HFI-35
SAA-R.P.
GQAP
Chron/RCN
Legal File/88-444-637
California State Food & Drug
L. A. Files

/dh/sk

CATALOG #8060

**HUMAN IMMUNODEFICIENCY
VIRUS TYPE 1
(HIV-1)**

Recombigen® - HIV-1 LA Test

**Recombinant Antigen -
Latex Agglutination Test
for the Detection of
Human Antibody to HIV-1**



**Cambridge
BioScience**

Cambridge BioScience Corporation
U.S. License Number 1063
365 Plantation Street
Worcester, MA 01605
(508) 797-5777
(800) 637-8376

Recombigen® is a Registered Trademark of Cambridge BioScience Corporation

**Human Immunodeficiency Virus Type 1 (HIV-1)
Recombinant[®]- HIV-1 LA Test**
Cambridge BioScience Corporation Latex Agglutination Test for the
Detection of Antibodies to Human Immunodeficiency Virus (HIV-1)

The apparent simplicity of this test does not obviate the need for users to develop the proficiency required for accurate interpretation of results. The agglutination patterns of this test differ from those of other latex tests. Strict adherence to the testing protocol is essential.

INTENDED USE

Cambridge BioScience Corporation Recombinant[®]-HIV-1 LA (Latex Agglutination) Test is a rapid *in vitro* qualitative assay for the detection of antibody to Human Immunodeficiency Virus Type 1 (HIV-1), which is also known as Lymphadenopathy Virus (LAV1) or Human T-lymphotropic Virus Type III (HTLV III). This test can be used by properly trained personnel as a screening test in hospital laboratories, medical clinics, physicians' offices, and emergency care situations, and in blood banks or other settings where enzyme immunoassays are not practical or available.

SUMMARY AND EXPLANATION OF THE TEST

Available data indicate that the acquired immunodeficiency syndrome (AIDS) is caused by a virus transmitted through sexual contact, exposure to blood (including sharing contaminated needles and syringes) or certain blood products, or transmitted from an infected mother to her fetus or child during the perinatal period.^{1,2} Human Immunodeficiency Virus Type 1 (HIV-1) has been isolated from patients with AIDS and AIDS-related complex (ARC) and from healthy persons at high risk for AIDS.³⁻¹¹ The incidence of antibodies specific for HIV-1 in AIDS and ARC patients and persons at increased risk for AIDS is high. The prevalence of HIV-1 infection in people not considered to be at increased risk is not known. The Cambridge BioScience Corporation Recombinant[®]-HIV-1 LA Test can rapidly detect antibodies to HIV-1. Non-specific reactions may be seen in some samples. As a consequence, it is necessary to investigate specimens found to be reactive by Recombinant[®]-HIV-1 LA Test in a manner that gives improved predictability that HIV-1 antibody, in fact, is present. When a specimen reacts in an initial test (is initially reactive), the Recombinant[®]-HIV-1 LA Test should be repeated in duplicate on the same specimen. The test, when reactive in either or both of these duplicate assays (repeatedly reactive) is highly predictive of the presence of antibody in people at increased risk for infection (e.g. homosexual men, hemophiliacs, or intravenous drug users) and are usually found to contain antibodies by additional more specific testing. However, when the Recombinant[®]-HIV-1 LA Test is used to screen populations in which the prevalence of HIV-1 infection is low, nonspecific reactions may be more common. Test results should be held confidential. Results should only be reported to the requesting health care professional. It has been established that repeatedly reactive units of blood and plasma should be eliminated from the blood supply.

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

Research has shown that antibodies against the HIV-1 *env* gene product can be found in nearly all infected people, and that highly sensitive diagnostic assays utilizing recombinant peptides derived from the *env* gene product can be developed.¹²⁻¹⁴

The recombinant antigen in this test contains the most important conserved and biologically functional regions of the *env* gene. It has been engineered to obtain high expression levels in *Escherichia coli* which allows the antigen to be efficiently purified to apparent homogeneity. The availability of pure *env* polypeptides in large quantities has made it possible to develop a rapid latex agglutination test for antibodies to HIV-1 with high sensitivity and specificity. The Recombinant[®]-HIV-1 LA test contains a colloidal suspension of latex beads coated with the purified Cambridge BioScience recombinant *env* polypeptide. Reaction with HIV-1 *env* antibodies causes cross-linking of the latex-antigen which results in a visual change in the bead suspension. The change, usually called agglutination, occurs within 3 minutes. The cross-linking can occur because antibodies have at least two "arms", each of which can bind with antigen. Thus one "arm" binds one bead and another binds a second bead.

In the presence of very high concentrations of HIV-1 antibody all the antigens on every bead may be reacted with specific immunoglobulin which would prevent the bridging of antibodies from one bead to another. This problem is obviated in the Recombigen system by predilution of the sample on the reaction card.

Inactivated seropositive human serum samples serve as the Positive Control. Seronegative human serum samples serve as the Negative Control. All reagents have been prediluted and are provided in ready to use format in plastic dropper bottles capable of delivering appropriate reaction volumes. All dilutions and mixing of the test sample occur directly on the agglutination card.

REAGENTS AND MATERIALS

Catalog #6060: Recombigen[®]-HIV-1 LA Test Kit

1. **Antigen coated latex beads, sufficient for 100 tests, 1 vial, 1.5 ml**
Diluted in buffer containing 0.1% sodium azide as a preservative.
2. **Sample Diluent, sufficient for 100 tests, 1 vial, 2.5 ml**
Buffer containing 1.0% bovine serum albumin and 0.1% sodium azide as a preservative.
3. **Positive Control, sufficient for 20 tests, 1 vial, 0.5 ml**
Inactivated human serum nonreactive for Hepatitis B surface antigen; containing antibodies to HIV-1 and diluted in a buffer with 0.1% sodium azide as a preservative.
4. **Negative Control, sufficient for 20 tests, 1 vial, 0.5 ml**
Normal human serum negative for antibody to HIV-1 and nonreactive for Hepatitis B surface antigen; diluted in a buffer containing 0.1% sodium azide as a preservative.
5. **Agglutination cards, each sufficient for 6 tests, 2 packages of 10 cards**
6. **Transfer Loops, 100 provided**
Calibrated to deliver the appropriate sample volume.
7. **Interpretation guide, 1 provided**
Photographs and descriptions of the latex agglutination reactions.

MATERIALS AVAILABLE SEPARATELY

Catalog #6340: Agglutination Cards
Package of 10 cards

Catalog #6342: Transfer Loops
Package of 100 loops

MATERIALS REQUIRED BUT NOT PROVIDED

1. HIV-1 Latex Agglutination Interpretation Panel. Users of the Recombigen® -HIV-1 LA Kit are required to use this panel to familiarize themselves with the agglutination reactions. The panel consists of five samples that react with HIV-1 antigen coated latex beads over a range of reactivity levels described in the HIV Latex Agglutination Interpretation Guide. It is particularly helpful to users who have not had experience interpreting latex agglutination reactions, as well as to those who are not familiar with the unique texture of the weakly positive reactions typical of this kit.
2. Disposable gloves
3. Biohazard discard bags, suitable for sterilization by autoclaving
4. Timer
5. High intensity light source or a magnified fluorescent lamp

OPTIONAL EQUIPMENT

1. Orbital rotator with humidified cover

WARNINGS AND PRECAUTIONS FOR USERS

The apparent simplicity of this test does not obviate the need for users to develop the proficiency required for accurate interpretation of results. The agglutination patterns of this test differ from those of other latex tests. Strict adherence to the testing protocol is imperative.

1. All of the reagents and materials provided are for *in vitro* diagnostic use.
2. Handle the specimens, human serum controls, and used materials as if they were capable of transmitting infection.
3. Do not smoke, eat or drink in areas where specimens or kit reagents are handled.
4. Avoid splashing or aerosol formation with samples.
5. Wear disposable gloves while handling samples and human serum positive control.
6. Do not use mouth pipetting techniques to transfer samples.
7. Dispose of all materials used to perform the test by autoclaving at 121°C for one hour. Spills should be wiped up using a 10% solution of household bleach, sodium hypochlorite (0.5%), alcohol (70%), or iodophor disinfectant.
8. Performance of the test is adversely affected by heat inactivation procedures, or by long term storage of samples. These types of samples as well as viscous specimens or specimens containing precipitate may give erroneous test results.

9. Avoid microbial contamination of reagents and samples.
10. Use a separate Transfer Loop for each sample and control. Cross contamination of samples will generate false results.
11. Do not interchange reagents from different lots.
12. Do not use the kit beyond the expiration date.
13. Agglutination of the latex beads by test samples demonstrates the presence of anti-HIV-1 antibody only and should not be considered as a diagnostic indication of acquired immunodeficiency syndrome. Such a diagnosis can only be made by a physician according to accepted medical criteria.
14. Do not touch circles on the agglutination cards. Fingerprints interfere with the test result.
15. Reagents containing sodium azide may react with lead and copper plumbing to form highly explosive metal azides. To dispose of solutions containing sodium azide, flush with a large volume of water to prevent azide accumulation.
16. Wash hands thoroughly after completion of assays.

STORAGE INSTRUCTIONS

Store all reagents at 2-8°C. Bring to room temperature (18° to 30°C) for approximately 30 minutes before use.

INDICATION OF INSTABILITY OR DETERIORATION

Positive Control Serum should give a weakly positive (1+ to 3+) agglutination reaction according to the Interpretation Guide and the Negative Control Serum should give no agglutination. Deterioration of the positive control serum may be seen on storage at reactivity of the positive control serum may be seen on storage at temperatures above 25°C. If either the positive or negative control does not give the proper result, the kit should not be used. In this situation, contact the Technical Service Department at Cambridge BioScience Corporation, (800) 627-8376 or (508) 797-5777 (in Massachusetts).

SPECIMEN COLLECTION AND PREPARATION

The Cambridge BioScience Corporation Recombigen® -HIV-1 LA Test is designed to be used with freshly collected capillary and venous whole blood, serum and plasma. Capillary samples must be immediately mixed with the Sample Diluent on the agglutination card as described in Step B8 of Qualitative Assay Procedure. Whole blood or plasma specimens must be collected properly into blood collection containers containing EDTA (1.5 mg per mL), heparin (15 USP Units per mL) or CPDA1 (63 mL per donor unit). Anticoagulated whole blood samples should be tested within 24 hours after drawing and samples should not be used if there is evidence of clotting. During the preparation of serum and plasma samples, carefully remove the sample to avoid collecting fibrin or other cellular debris (see section on limitations).

Store serum or plasma specimens refrigerated (2-8°C) for no more than 5 days or frozen. Store whole blood refrigerated not longer than 24 hours and do not freeze. The adverse effects of long term freezer storage on sample reactivity have not been characterized. Do not use a freezer with a frost free cycle. Shipped specimens should be packaged in compliance with Federal regulations covering the transportation of etiologic agents.

QUALITATIVE ASSAY PROCEDURE

Preliminary Comments:

Users of the Recombigen® HIV-1 LA Test Kit are required to have used the HIV Latex Agglutination Interpretation Panel to familiarize themselves with agglutination reactions. It is particularly helpful to users who have not had experience interpreting latex agglutination reactions, as well as those who are not familiar with the unique texture of the weakly positive reactions of this kit.

Procedure:

1. Allow reagents to reach room temperature (18 to 30°C) before use.
2. Record patient sample identification on the blue border of the latex agglutination card.
3. Vortex or vigorously mix the antigen coated latex beads to ensure that the latex suspension is homogeneous.
4. Before dispensing reagents and controls, remove outer bottle cap and inner tip protector and wipe the outer tip to remove any liquid that may have adhered to the tip.

Note: In order to deliver consistent and accurate volumes of reagents, wipe the tip as often as necessary to keep it dry; while dispensing reagents, invert the bottle and hold in a vertical position; gently squeeze the bottle and allow drop to form on the tip. Avoid using drops with air bubbles and allow drops to fall freely from the tip. Keep the bottle in the vertical position until you have dispensed the reagent onto all appropriate reaction circles on the agglutination card.

5. Apply one drop (~25 µl) of the Negative Control to circle number 5 on each agglutination card to be used. *No more than two (2) cards should be used at one time, and a negative control must be run on each card.* Using a new transfer loop, spread the control over the entire surface area enclosed by the indicator circle. Immediately discard the transfer loop into a biohazard bag.
6. Apply one drop (~25 µl) of the Positive Control to circle number 6 on each agglutination card to be used. *A positive control must be run on each card.* Using a new transfer loop, spread the control over the entire surface area enclosed by the indicator circle. Immediately discard the transfer loop into a biohazard bag.
7. Apply one drop (~25 µl) of Sample Diluent to circles number 1, 2, 3 and 4 on the agglutination card.

8. A. Venous whole blood, serum, plasma

Using a separate transfer loop for each test sample, dip the loop into a sample to be tested. Twirl the loop to ensure that a bubble has not blocked the sampling loop. The transfer loop will pick up an appropriately sized sample to yield a final dilution of approximately 1:10 of the sample. Use the transfer loop to mix the sample aliquot with the drop of Sample Diluent on the agglutination card. Spread each sample over the entire surface area enclosed by the indicator circle. Flip the loop over and continue spreading; this procedure ensures accurate dilution of the test sample. Immediately discard each transfer loop into a biohazard bag.

B. Capillary whole blood

When testing capillary samples, clean skin surface well with alcohol, wipe with sterile gauze and puncture with a sterile lancet. Wipe away first drop of blood and allow a second to form. Dip a clean transfer loop into the drop of blood as soon as it has formed and immediately transfer it to an agglutination card containing one drop of Sample Diluent (step 7). Spread the sample over the entire surface area of the circle, flip the loop and continue mixing. Immediately discard each transfer loop into a biohazard bag.

9. Apply one drop (~15 µl) of well mixed latex bead suspension to each sample and control on the agglutination card.
10. Rock and rotate slowly with a figure eight motion for 3 minutes (but no longer than 5 minutes) preferably in a humidified atmosphere. A mechanical orbital rotator at 30-60 rpm may be used for this motion. A horizontal rotator may be used but gives less satisfactory results. **Note:** When using a rotator in a biological safety cabinet, a humidified cover should be used to prevent the reagents from drying on the card.
11. Stop rotation and immediately (in ~30 to 60 seconds) assess the agglutination reactivity of the samples versus the negative controls. Observe agglutination patterns while hand rotating the agglutination card. Positive samples will contain small homogeneous grains of agglutination that move throughout the reaction circle as the card is rotated. Refer to the following section and/or the HIV-1 Latex Agglutination Interpretation Guide for descriptions and pictures of typical latex reactions.
12. Record agglutination scores for each patient sample.
13. Discard the agglutination card into a biohazard bag.

INTERPRETATION OF THE TEST RESULTS

A positive reaction is defined as agglutination visible in a bright light which is greater than that seen with the negative control. A negative reaction is characterized by the lack of visible agglutination; the liquid will retain a smooth, milky white appearance similar to the negative control.

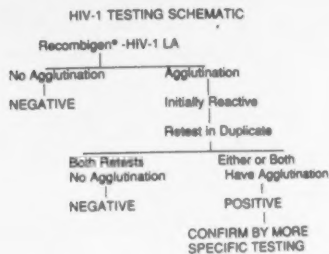
Although direct sunlight is sufficient, standard fluorescent room lighting is insufficient to examine agglutinations. A magnified fluorescent lamp or a high intensity lamp allow the best visualization of the agglutination reaction.

Occasional drying of the latex bead suspension on the interior of the bottle tip or cap may result in the appearance of white particulates which tend to localize in the center of the reaction circle. Proper handling of dropper tips and bottles will minimize the occurrence of these particulates (see note in Step 4). Particulates should not be interpreted as agglutination; agglutination appears uniformly over the entire reaction circle.

Refer to the HIV Latex Agglutination Interpretation Guide for descriptions and pictures of typical latex agglutination reactions. Specimens with agglutination greater than the negative control are considered initially reactive for antibodies to HIV-1 and should be retested in duplicate. If either duplicate retest is reactive, the specimen is considered repeatedly reactive and should be interpreted as positive by the Recombigen® -HIV-1 LA Test.

Initially reactive specimens which do not repeat in either of the duplicate repeat tests are considered negative for antibodies to HIV-1.

Specimens found to be repeatedly reactive by Recombigen® -HIV-1 LA Test and positive by additional more specific testing are considered positive for antibodies to HIV-1. The interpretation of results of specimens found repeatedly reactive by Recombigen® -HIV-1 LA Test and indeterminate on additional more specific testing is unclear; further clarification may be obtained by testing another specimen taken three to six months later.



7

LIMITATIONS OF THE PROCEDURE

The Cambridge BioScience Corporation Recombigen® -HIV-1 LA Test procedure and the Interpretation of Results descriptions must be followed closely when testing for the presence of antibodies to HIV-1 in blood, plasma or serum from individual subjects. Because Recombigen® -HIV-1 LA was designed to test fresh serum, blood or plasma, data supporting use of the test were derived from testing individual samples.

Insufficient data are available to support use with other body specimens, processed plasma, and products made from such pools. Pooled samples may yield false-positive and false-negative results. Testing of these specimens is not recommended.

Reduced sensitivity has been observed with samples from infants under two years of age. Heat inactivation of samples has been shown to result in a 2 to 8 fold decrease in titer after heating to 56°C for 30 minutes, possibly due to heat induced denaturation of agglutinating antibodies. Testing of heat inactivated samples is not recommended. Do not test samples that have been precipitated in serum, contaminated with bacteria, or are hyperlipemic. Testing serum or plasma specimens stored for more than 5 days at 2-8°C, 6 months frozen, or repeatedly frozen and thawed is not recommended. Samples stored under these conditions as well as samples containing precipitates may give erroneous results.

The Cambridge BioScience Corporation Recombigen® -HIV-1 LA Test is a rapid test to detect antibodies to HIV-1 in blood, serum and plasma and can be used by properly trained personnel as a screening test in hospital laboratories, medical clinics, physicians' offices, and emergency care situations, and in blood banks or other settings where enzyme immunoassays are not practical or available. Clinical studies continue to clarify and refine the interpretation and medical significance of the presence of antibodies to HIV-1.¹⁵⁻¹⁷ It is recommended that repeatedly reactive specimens be investigated by an additional more specific test. A person who has antibodies to HIV-1 is presumed to be infected with the virus and appropriate confidential counseling and medical evaluation should be offered. Such an evaluation should be considered an essential part of HIV-1 antibody testing and should include test result confirmation on a freshly drawn sample.

AIDS and AIDS-related conditions are clinical syndromes and their diagnosis can only be established clinically.^{18,19} The Recombigen® -HIV-1 LA Test alone cannot be used to diagnose AIDS, even if the recommended investigation of reactive specimens suggests a high probability that the antibody to HIV-1 is present. The lifetime risk of an asymptomatic person confirmed as having antibodies to HIV-1 developing AIDS or an AIDS-related condition is not known.^{20,21}

A negative test result at any point in the investigation of individual subjects does not preclude the possibility of exposure to, or infection with, HIV-1.

8

EXPECTED RESULTS AND SPECIFIC PERFORMANCE CHARACTERISTICS

A. Sensitivity and Specificity Data:

Test performance of Recombigen® -HIV-1 LA was investigated in parallel with licensed EIA tests in clinical studies at multiple sites.

Sensitivity was computed based on the clinical diagnosis of AIDS. Specificity was computed based on testing random donors in licensed blood and plasma collection centers.

Sensitivity, based on an assumed 100% prevalence of HIV-1 antibody in persons diagnosed as having AIDS, was 99.4% (Table 1).

Specificity, based on an assumed zero prevalence of HIV-1 antibody in random U.S. blood donors, was 99.5% (Table 3).

Specificity was also estimated in a physician's office and two hospital emergency rooms and ranged between 88.7% and 98.0% (Table 4). Reduction of test specificity for samples tested in these settings may be related to user training and proficiency. False positive tests may also occur in certain medical conditions (Table 2).

B. Rate of Reactivity in Patient Populations

The rate of reactivity of the Recombigen® -HIV-1 LA for serum and plasma specimens from patients diagnosed as having AIDS and from persons with other diseases and medical conditions unrelated to HIV-1 infection are shown in Tables 1 and 2, respectively.

TABLE 1
Detection of Antibody to HIV-1 in Serum and Plasma Samples from Patients with AIDS

Group	Recombigen® -HIV-1 LA				Licensed EIA ^a			
	No. of Specimens Tested	Initially Reactive	Repeatably Reactive	% Repeatably Reactive	Initially Reactive	Repeatably Reactive	% Repeatably Reactive	
AIDS	163	162	162 ^b	99.4	163	163	100.0	

a. Licensed, whole virus antigen EIA testing varied according to testing site.

b. One sample, nonreactive at the site, was repeatably reactive when retested under code at Cambridge BioScience.

TABLE 2
Rate of Reactivity of Recombigen® -HIV-1 LA on EIA Seronegative Samples from Persons with Other Diseases or Medical Conditions Unrelated to HIV-1 Infection^a

Condition	Number Tested	Initially Reactive	Repeatably Reactive	% Repeatably Reactive
ANA	20	2	2	10.0
Rheumatoid Factor	25	1	1	4.0
EBV	15	0	0	0.0
Hepatitis B ^b	24	2	1	4.2
CMV	311	7	3	1.0
Rubella AB	8	3	1	12.5
Myeloma	18	5	2	11.1
HLA AB	10	0	0	0.0
HTLV-1 AB	17	3	3	17.6
E. coli Infections	38	5	3	7.9

a. Some of the samples were tested at Cambridge BioScience, but the majority were tested at various clinical sites.

b. 1 HBeAg only, 2 HBeC-CMV, 3 HBeC only, 2 HBeAg only, 1 HBeAg-HBeAS-HBeC, and 1 HBeAS-HBeC-CMV.

These samples were not included in the other categories.

C. Rate of Reactivity in Random Donor Populations

The ability of Recombigen® -HIV-1 LA to detect antibody to HIV-1 in blood bank donor specimens is shown in Table 3.

TABLE 3
Rate of Reactivity in Random Donor Populations

Site	Number Tested	Recombigen® -HIV-1 LA		Licensed EIA ^a	
		Initially Reactive	Repeatably Reactive	Initially Reactive	Repeatably Reactive
Blood Bank 1	1011	5 (0.5%)	5 (0.5%)	11 (1.1%)	0 (0.0%)
Blood Bank 2	1000	4 (0.4%)	4 (0.4%)	4 (0.4%)	4 (0.4%)
Blood Bank 3	980	5 (0.5%)	5 (0.5%)	1 (0.1%)	0 (0.0%)
TOTAL	2991	14 (0.5%)	14 (0.5%)	16 (0.5%)	4 (0.1%)

a. Licensed whole virus antigen EIA test kits varied according to testing site.

b. Western blot and/or RIP assays were performed on all samples repeatably reactive by Recombigen® -HIV-1 LA or EIA. All EIA repeatably reactive samples had antibodies to envelope by Western blot or RIP and to at least one other viral band by Western blot. The Recombigen® -HIV-1 LA was repeatably reactive for these same samples in all cases.

In Blood Bank 3, 336 donors had paired samples tested both as serum and plasma. One sample was repeatably reactive as plasma but negative as serum, and another sample was repeatably reactive as serum but not plasma. Neither sample was positive by Western blot. This showed the equivalent specificity of testing serum vs plasma.

D. Rate of Reactivity in Populations Tested at Outpatient Clinics, Emergency Rooms, and a Physician's Office

The ability of Recombigen®-HIV-1 LA to detect antibody to HIV-1 in specimens from selected outpatient clinics, emergency rooms, and a physician's office is shown in Table 4.

TABLE 4
Rate of Reactivity in Populations Tested at Outpatient Clinics, Emergency Rooms, and a Physician's Office

Site	Number Tested	Recombinogen® HIV-1 LA		Licensed EIA ^a	
		Initially Reactive	Repeatably ^b Reactive	Initially Reactive	Repeatably ^b Reactive
Physician's Office	102	12 (11.8%)	10 (10.9%)	1 (1.0%)	0 (0.0%)
Emergency Room 1	100	2 (2.0%)	2 (2.0%)	1 (1.0%)	0 (0.0%)
Emergency Room 2	53	10 (18.9%)	8 (15.1%)	1 (1.9%)	1 (1.9%)
High Risk Clinic 1	159	83 (52.2%)	83 (52.2%)	84 ^c (52.8%)	Not done
High Risk Clinic 2	49	21 (42.9%)	21 (42.9%)	19 (38.8%)	19 (38.8%)
High Risk Clinic 3	34	29 (85.3%)	29 (85.3%)	29 ^d (85.3%)	Not done
High Risk Clinic 4	18	16 (88.9%)	16 (88.9%)	16 (88.9%)	16 (88.9%)

- a. Licensed whole virus antigen EIA test kits varied according to testing site.
 b. Western blot and/or RIP assays were performed on all samples repeatably reactive by Recombigen®-HIV-1 LA or EIA. All EIA repeatably reactive samples had antibodies to envelope by Western blot or RIP and to at least one other viral band by these same samples in all cases.
 c. EIA not repeated, but in 83 samples in Clinic 1 and 29 samples in Clinic 3 had env and at least one other viral band by Western blot.
 d. EIA not repeated, but in 83 samples in Clinic 1 and 29 samples in Clinic 3 had env and at least one other viral band by Western blot.

E. Reactivity of Recombigen®-HIV-1 LA with Six Seroconversion Panels

The Recombigen®-HIV-1 LA Test detected the presence of HIV-1 antibody as early or, in some instances, earlier than a licensed EIA in seroconversion panels. The ability of Recombigen®-HIV-1 LA to detect antibody to HIV-1 in six commercially available seroconversion panels is shown in Table 5.

TABLE 5
Rate of Reactivity of Recombigen®-HIV-1 LA in Seroconversion Panels^a

Panel/Panel	Recombinogen® HIV-1 ^b	FDL Licensed EIA ^c	FDL Licensed Blot ^d
A1 (0) ^e	N ^f	0/3 ^g	weak 24 ^f
A2 (65)	N	0/3	weak 24 ^f
A3 (86)	3+	1/3	weak 24 ^f
A4 (107)	2+	3/3	24, 120/160
C1 (0)	N	0/3	N
C2 (7)	N	0/3	N
C3 (9)	1+	1/3	w24, w160
C4 (14)	2+	1/3	24, 160
C5 (16)	2+	1/3	24, 160
C6 (21)	2+	3/3	24, 160
D1 (0)	N	0/1	nd ^g
D2 (21)	N	0/1	nd
D3 (49)	N	0/1	N
D4 (99)	3+	1/1	17,24,31,41,53, 55,66,120,160
D5 (106)	3+	1/1	nd
E2 (0)	N	0/1	weak 17 ^f
E6 (42)	N	0/1	weak 17 ^f
E9 (82)	N	0/1	weak 17 ^f
E10 (115)	4+	1/1	17,24,31,41,53, 55,66,120,160
F68 (0)	N	0/1 ^g	N
F69 (6)	N	0/1	N
F70 (21)	1+	0/1	24
F71 (28)	2+	1/1	24
M1 (0)	N	0/1	N
M2 (30)	4+	1/1	17,24,31,41,53, 55,66,120,160

- a. Bioness Biotechnology, Inc., West Bridgewater, MA, USA.
 b. Performed by Cambridge BioScience.
 c. Days after first bleeding.
 d. Negative.
 e. Number of different licensed EIA kits (positive/negative tests tested).
 f. Bands did not change in intensity. Sample A3 had antibodies to gp 160 by RIP.
 g. Not done.

F. Precision

Assay reproducibility was determined by assaying a panel of 3 positive and 97 negative samples 9 times by 11 operators at 7 sites. All readings are summarized in Table 6.

TABLE 6
Recombinant[®] HIV-1 LA Reproducibility

Expected Result	No. of Samples	No. of Repeat Tests	Reader Results				
			N	+	±	-	±
N	97	922	864	50	5	3	0
2 ± 1	1	22	0	0	13	7	2
3 ± 1	1	21	1	0	3	12	5
4 ±	1	23	0	0	1	0	22

G. Use of Plasma, Capillary and Venous Whole Blood as Specimens Collected in Various Anticoagulants

Recombinant[®] HIV-1 LA Test was performed using matched serum and plasma samples from 29 individuals utilizing EDTA (15 mg/dl), heparin (15 USP units/mL), and CPD (63 mL per donor unit) as anticoagulants. There was 100% agreement for reactive samples, and 99.5% agreement for nonreactive samples.

Venous whole blood and capillary (fingertick) samples were compared to matched serum samples from 19 seropositive persons and 98 seronegative persons. Overall agreement was 100.0%.

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SUBMISSION FOR THE RECORD
 HEARING BEFORE THE
 SUBCOMMITTEE ON REGULATION,
 BUSINESS OPPORTUNITIES, AND ENERGY
 COMMITTEE ON SMALL BUSINESS
 U.S. HOUSE OF REPRESENTATIVES
 MARCH 23, 1989
 "AIDS TESTING"

In FY 1989, it is estimated that 64 staff years will be dedicated to health fraud work. Of these, we expect that half will be specifically related to AIDS. In deploying these resources, 18 staff years will be utilized in headquarters and 46 staff years will be devoted to activities by investigators and others in field locations nationwide.

N A T I O N A L
NGLTF
 G A Y & L E S B I A N
 T A S K F O R C E

Statement on Home HIV Testing

Jeffrey Levi

Executive Director

March 24, 1989

House Committee on Small Business

Subcommittee on Regulation and Business Opportunities

Mr. Chairman, on behalf of the National Gay and Lesbian Task Force, the oldest national gay and lesbian advocacy organization, I want to thank you for your leadership in highlighting the very significant concerns associated with home testing for HIV.

We come to this issue with a special understanding of the public health significance of the HIV epidemic. An understandably frightened public is looking for every means possible to control the spread of HIV. We firmly believe that every individual should have every opportunity to be fully informed about his or her HIV status. But the emphasis must be on the word fully. We believe that the technological limitations of home testing and the lack of quality counseling this approach implies prevent individuals from being fully informed.

In considering the place of home testing in our battle against AIDS, we must remember that not all technology is as great as we would want it to be -- or as manufacturers interested in profit would have us believe. And simply because a technology exists, its value must be assessed in a larger social context. Policy objectives should drive the uses of technology, not vice versa. It is these two issues that force us to oppose the use of home-based test kits at this time.

When the HIV antibody test known as the ELISA was first released, its accuracy was not as great as it is today. We did not initially have a confirmatory test as we do today in the Western Blot. The technology was adequate for its initial purpose: to screen blood products rather than give individuals information about their health status. We opposed widespread testing outside the blood bank setting before the technology improved. Now that the combination of ELISA and Western Blot assures us that an individual being tested will get an accurate assessment of his or her HIV status, we no longer oppose widespread availability of the option to be tested. But as long as there was the danger of a high false positive rate -- which there seems to be at this stage of the home-testing technology -- we believed that more harm than good might be done if a significant number of people might be misled about their status.

AIDS and HIV infection are very serious conditions. The implications for one's life are obvious. The psychological impact of such a result is understandably staggering. Many have attempted suicide upon learning of infection. We are deeply concerned that making a home-test available with a relatively high false positive rate might well be irresponsible in playing with the emotions of already frightened and concerned individuals. If we did not have an alternative, higher quality test available, a less accurate test might be acceptable. But this is clearly not the case today.

Every public health official in this country and around the world has argued that testing alone is not the key to controlling the AIDS epidemic. All testing should be accompanied by counseling: about one's risk, about the meaning of the test, and the appropriate follow-up medically and behaviorally if one tests positive. Testing does not occur in a vacuum. It is most effective when accompanied by quality counseling -- counseling that is best provided and assured in person.

We are deeply concerned that those seeking testing through home test kits will not receive the pre- and post-test counseling that is the standard policy of every public health agency in this nation. We have yet to hear from the home-test manufacturers how they are going to match the quality and quantity of counseling offered under the current testing system. Until they come closer to the standards set by public health agencies from the Centers for Disease Control on down -- then we fear that the prevention value of testing will be diminished and the negative psychological consequences of testing will be greater.

There is no doubt that there will be a demand for home testing services. We believe that the government has a responsibility to protect unwary and frightened consumers from products that might compound, not ameliorate, the HIV epidemic and its social consequences. If we need to find more confidential and attractive means for making existing, quality testing available, then we should do so -- not by licensing less accurate tests, but by expanding the number of alternative testing sites available.

Mr. Chairman, we do not desire to stand in the way of new technologies. We do, however, want to make sure that the new technologies are indeed better than the old and that the social context into which they will be placed is adapted to take these changes into account. Unfortunately, we believe the accuracy and the counseling issues associated with home tests today call for a delay in their availability. When these issues are addressed, we will join in welcoming them as another tool in our fight against this awful epidemic.

Thank you again for your leadership in this area.



PSYCHIATRY

UNIFORMED SERVICES UNIVERSITY OF THE HEALTH SCIENCES
F. EDWARD HÉBERT SCHOOL OF MEDICINE
4301 JONES BRIDGE ROAD
BETHESDA, MARYLAND 20814-4799

17 April 1989



TEACHING HOSPITALS
WALTER REED ARMY MEDICAL CENTER
NAVAL HOSPITAL, BETHESDA
MALCOLM GROW AIR FORCE MEDICAL CENTER
WILFORD HALL AIR FORCE MEDICAL CENTER

Ron Wyden
Chairman
United States House Of Representatives
Committee on Small Business
Subcommittee on Regulation, Business
Opportunities, and Energy
B-363 Rayburn House Office Building
Washington DC 20515

Dear Congressman Wyden,

It was a pleasure to testify at the March 23, 1989 hearing convened by the House Subcommittee on Regulation, Business Opportunities, and Energy to examine potential concerns and risks associated with the manufacture and marketing of AIDS home test kits. I am happy to answer the additional questions of the subcommittee in your letter dated April 11, 1989 to supplement my testimony.

Question 1. You stated in your testimony that the Air Force has documented a suicide attempt rate of infected HIV patients at least 40 times higher than that of the Air Force in general. Could we expect a similar, or greater proportion among the general population if AIDS home testing kits were available?

Suicides and suicide attempts are potential negative outcomes of a home testing program. Suicide rates in civilians with AIDS are up to 66 times that of the general population and 36 times that of individuals who are the same gender and age. Our experience with suicide attempts in patients at early stages of HIV infection has been of the same magnitude. Our examinations of randomly selected patients reveals that almost one in five admits to at least considering suicide as a potential option over the next year.

There is, of course, no way to prospectively predict a suicide or suicide attempt rate in a yet-to-be-defined population, namely those individuals who would find out they have a positive result on a home AIDS test kit. There are forces in two different directions that make it hard to compare those potential individuals with our patient population. In the direction of predicting a lower suicide risk in nonmilitary individuals is the fact that military



personnel take the test because it is mandatory. They do not necessarily want to know their serologic status. Individuals who use home AIDS test kit would presumably do so voluntarily. In the direction of predicting a higher suicide risk in the general population is the fact that our population has more job/income security, less drug abuse, and is more likely to be married than civilians who are HIV-seropositive. In addition, in the military we provide annual comprehensive medical evaluations and counselling and, when felt to be indicated, intervening medical or psychiatric followup. Such precautions and safeguards would be absent in a home testing program.

=====

Question 2. How projectable are your findings to the general population?

Many of the points made in the answer to Question 1 also apply here. There is an important difference between our population and individuals who might use a home AIDS test. Military personnel take the test because they are required to do so. However, no one knows who would take a home AIDS test or for what reasons. Individuals with psychiatric disorders, irrational fears, or phobias are likely to use this test in very idiosyncratic ways. This may or may not be a small number of people; but the stakes are higher than with the home pregnancy test or home tests for blood in the stool. Further research is needed just to define the psychiatric problems associated with testing for such a fatal condition, before we are able to define solutions.

=====

Question 3. You believe that increasing the availability and duration of counselling is a key factor if suicides are to be prevented. Do you believe that a viable telephone counselling network can be established which will increase the availability and duration of counselling?

In mental health screening and evaluation, examination of visual data such as general appearance, tearfulness, facial expressions, eye contact, posture, and grooming are integral parts of the examination. These important parts of an evaluation cannot be conducted over the telephone. When suicide hotlines exist they are there out of necessity; counsellors who staff those phone lines are familiar with the resources of a local community. A centralized toll-free telephone line can't have available more than a skeleton outline of a given community's medical and mental health referral resources.

=====

Question 4. Would you recommend, based on your experience, that changes should be made in the amount and types of counselling and mental health services available to HIV positive individuals?

In the Air Force our efforts have been in the direction of trying to make more mental health resources available to HIV-seropositive persons for longer periods of time. It has never been a consideration for us that face-to-face patient contact could be effectively replaced by the telephone.

=====

Question 5. How persistent are the mental health problems of HIV-infected personnel? Are these problems that appear soon after the test and then go away or do they persist over a long period of time?

We have found in our research only a modest difference in the frequency of psychiatric disorders and in measures of psychological distress between individuals who have just found out they are HIV-seropositive and individuals who have known for one year. Though most Air Force personnel who are notified of their seropositive status adjust well, knowledge of this state carries with it emotional consequences that are sometimes severe, and when present, persistent. We frequently arrange psychiatric followup for HIV-infected individuals following their initial medical evaluation.

=====

Question 6. What determines how an individual will react to the knowledge of HIV infection?

The emotional reaction to this knowledge depends on a number of factors, including the amount of stigma perceived, availability of social supports, whether there is a pre-existing psychiatric disorder such as alcoholism or depression, and the biological effects of the virus on the brain. The reaction to news of seropositivity is very much individualized and complex. Counsellors often refer patients to psychiatrists to help sort through these complex determinants.

=====

Question 7. Would you characterize the current system of mental health care for persons who are infected with the virus, either in the military, or elsewhere, as adequate?

I wish to emphasize that I am a physician and clinician, not an expert in medical administration. There

have been frequent statements made in the civilian community about shortages of medical care facilities, housing, sources of income, and mental health care for AIDS and HIV-infected persons. As the burden of hospital care for AIDS patients increases over the next few years the impact on our medical care delivery systems (both military and civilian) will be substantial.

In the military, I have not yet personally had difficulty getting followup care arranged for HIV-seropositive individuals within our health care system. The problem has been getting the patients to go. Their major problems are those of stigma and real and perceived confidentiality violations. It is not clear not how much of a problem this would be among civilians who use home AIDS test kits. However, persons who are hesitant to go to an existing anonymous HIV test site for their test may also be hesitant to follow up on telephone recommendations for medical and mental health care.

=====

Question 8. To a layperson, the statistics you present in your statement about suicide among HIV positives are rather alarming. As a professional, who I assume deals with suicide on a more regular basis than most of us, do these statistics seem unique, special, or especially disturbing?

We are aware of two completed suicides in approximately 900 HIV-infected persons in the Air Force. This low number is hard to compare to other populations. However, the number of suicide attempts is historically high for the military and concerns us a great deal. And this number represents only those attempts we know about. To help put this in perspective, the rate of suicide attempts recorded in this population is in the same ballpark as that recorded for the highest other medical population we know about, persons with chronic renal failure who are on dialysis. This is an important area requiring further research.

=====

Question 9. In your experience with HIV-infected individuals, can you envision that a telephone-based counselling effort would be effective in addressing the mental health problems you describe?

The answer to Question 3, above, also applies directly to the issue raised in this question. We devote a large amount of time in the military attending to the large and growing mental health needs of the active-duty and medically retired HIV-seropositive population. It is difficult to envision accomplishing the necessary interventions by telephone. When Air Force personnel are psychiatrically examined at their annual medical evaluation and need

followup at their home base, we are able to set up that appointment over the phone. However, before making the necessary call we have completed a face-to-face examination of the individual, know he is not an imminent risk to himself or others, are very familiar with the military mental health referral resources, and don't do counselling over the phone. I am not aware of medical precedent for this type of activity. Suicide hotlines may come the closest, but they are resources of last resort, not first resort.

=====

I hope these answers to your thoughtfully posed questions will help the Subcommittee in its examination of potential concerns and risks associated with proposed home AIDS test kits. If you have any questions, please contact me at 295-2470.

Sincerely,

James R. Rundell, M.D.

James R. Rundell, M.D.
Major, USAF, Medical Corps
Assistant Professor
Department of Psychiatry
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4301 Jones-Bridge Road
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DEPARTMENT OF THE AIR FORCE
WASHINGTON, D.C. 20330

OFFICE OF THE SECRETARY

17 May 89

The Honorable Ron Wyden
House Committee on Small Business
Chairman, Subcommittee on
Regulation, Business Opportunities
and Energy
Washington, D.C. 20515

Dear Mr. Wyden:

Attached is a copy of a statement and inserts provided by Major James Rundell, of the Uniform Services University of the Health Science School of Medicine, per your request. Both have been routed through Secretary of Defense and Secretary of the Air Force Security Review channels and are cleared for public release.

I trust the foregoing is helpful to you.

Sincerely,

A handwritten signature in dark ink, appearing to read "Frank J. McKeown".
FRANK J. McKEOWN, Colonel, USAF
Legislation Division
Office of Legislative Liaison

2 Attachment

INSERT FOR THE RECORD					
☒ HOUSE	APPROPRIATIONS COMMITTEE	☐ HOUSE	ARMED SERVICES COMMITTEE	☒ HOUSE	OTHER
☐ SENATE		☐ SENATE		☐ SENATE	
HEARING DATE 23 Mar 89		TRANSCRIPT PAGE NO.		LINE NO.	
				INSERT NO. 89-01	

Mr. Wyden: You stated in your testimony that the Air Force has documented a suicide attempt rate of infected HIV patients at least 40 times higher than that of the Air Force in general. Could we expect a similar, or greater proportion among the general population if AIDS home testing kits were available?

Major Rundell: Suicides and suicide attempts are potential negative outcomes of a home testing program. Suicide rates in civilians with AIDS are up to 66 times that of the general population and 36 times that of individuals who are the same gender and age. Our experience with suicide attempts in patients at early stages of HIV infection has been of the same magnitude. Our examinations of randomly selected patients reveals that almost one in five admits to at least considering suicide as a potential option over the next year.

There is, of course, no way to prospectively predict a suicide or suicide attempt rate in a yet-to-be-defined population, namely those individuals who would find out they have a positive result on a home AIDS test kit. There are forces in two different directions that make it hard to compare those potential individuals with our patient population. In the direction of predicting a lower suicide risk in nonmilitary individuals is the fact that military personnel take the test because it is mandatory. They do not necessarily want to know their serologic status. Individuals who use home AIDS test kit would presumably do so voluntarily. In the direction of predicting a higher suicide risk in the general population is the fact that our population has more job/income security, less drug abuse, and is more likely to be married than civilians who are HIV-seropositive. In addition, in the military we provide annual comprehensive medical evaluations and counseling and, when felt to be indicated, intervening medical or psychiatric follow-up. Such precautions and safeguards would be absent in a home testing program.

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☒	HOUSE	APPROPRIATIONS COMMITTEE	☐	HOUSE	ARMED SERVICES COMMITTEE	☒	HOUSE	OTHER
	SENATE		☐	SENATE		☐	SENATE	
HEARING DATE		TRANSCRIPT PAGE NO.		LINE NO.		INSERT NO.		
23 Mar 89						89-02		

Mr. Wyden: How projectable are your findings to the general population?

Maj Rundell: Many of the points made in the answer to Question 1 also apply here. There is an important difference between our population and individuals who might use a home AIDS test. Military personnel take the test because they are required to do so. However, no one knows who would take a home AIDS test or for what reasons. Individuals with psychiatric disorders, irrational fears, or phobias are likely to use this test in very idiosyncratic ways. This may or may not be a small number of people; but the stakes are higher than with the home pregnancy test or home tests for blood in the stool. Further research is needed just to define the psychiatric problems associated with testing for such a fatal condition, before we are able to define solutions.

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HEARING DATE		TRANSCRIPT PAGE NO.		LINE NO.		INSERT NO.		
23 Mar 89						89-03		

Mr. Wyden: You believe that increasing the availability and duration of counseling is a key factor if suicides are to be prevented. Do you believe that a viable telephone counseling network can be established which will increase the availability and duration of counseling?

Maj Rundell: In mental health screening and evaluation, examination of visual data such as general appearance, tearfulness, facial expressions, eye contact, posture, and grooming are integral parts of the examination. These important parts of an evaluation cannot be conducted over the telephone. When suicide hotlines exist they are there out of necessity; counselors who staff those phone lines are familiar with the resources of a local community. A centralized toll-free telephone line can't have available more than a skeleton outline of a given community's medical and mental health referral resources.

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☐ SENATE		☐ SENATE		☐ SENATE	Comm on Small Business	
HEARING DATE 23 Mar 89		TRANSCRIPT PAGE NO.		LINE NO.	INSERT NO. 89-04	

Mr. Wyden: Would you recommend, based on your experience, that changes should be made in the amount and types of counseling and mental health services available to HIV positive individuals?

Maj Rundell: In the Air Force our efforts have been in the direction of trying to make more mental health resources available to HIV-seropositive persons for longer periods of time. It has never been a consideration for us that face-to-face patient contact could be effectively replaced by the telephone.

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HEARING DATE	TRANSCRIPT PAGE NO.	LINE NO.	INSERT NO.	Comm on Small Business	
23 Mar 89			89-05		

Mr. Wyden: How persistent are the mental health problems of HIV-infected personnel? Are these problems that appear soon after the test and then go away or do they persist over a long period of time?

Maj. Rundell: We have found in our research only a modest difference in the frequency of psychiatric disorders and in measures of psychological distress between individuals who have just found out they are HIV-seropositive and individuals who have known for one year. Though most Air Force personnel who are notified of their seropositive status adjust well, knowledge of this state carries with it emotional consequences that are sometimes severe, and when present, persistent. We frequently arrange psychiatric follow-up for HIV-infected individuals following their initial medical evaluation.

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☐ SENATE		☐ SENATE		☐ SENATE	Comm on Small Business	
HEARING DATE 23 Mar 89		TRANSCRIPT PAGE NO.	LINE NO.	INSERT NO. 89-06		

Mr. Wyden: What determines how an individual will react to the knowledge of HIV infection?

Maj Rundell: The emotional reaction to this knowledge depends on a number of factors, including the amount of stigma perceived, availability of social supports, whether there is a preexisting psychiatric disorder such as alcoholism or depression, and the biological effects of the virus on the brain. The reaction to news of seropositive is very much individualized and complex. Counselors often refer patients to psychiatrists to help sort through these complex determinants.

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HEARING DATE	TRANSCRIPT PAGE NO.	LINE NO.	INSERT NO.		
23 Mar 89			89-07		

Mr. Wyden: Would you characterize the current system of mental health care for persons who are infected with the virus, either in the military, or elsewhere, as adequate?

Maj Randell: I wish to emphasize that I am a physician and clinician, not an expert in medical administration. There have been frequent statements made in the civilian community about shortages of medical care facilities, housing, sources of income, and mental health care for AIDS and HIV-infected persons. As the burden of hospital care for AIDS patients increases over the next few years the impact on our medical care delivery systems (both military and civilian) will be substantial.

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☐ SENATE		☐ SENATE		☐ SENATE	
HEARING DATE 23 Mar 89	TRANSCRIPT PAGE NO.	LINE NO.	INSERT NO. 89-08		

Mr. Wyden: To a layperson, the statistics you present in your statement about suicide among HIV positives are rather alarming. As a professional, who I assume deals with suicide on a more regular basis than most of us, do these statistics seem unique, special, or especially disturbing?

Maj. Rundell: We are aware of two combined suicides in approximately 900 HIV-infected persons in the Air Force. This low number is hard to compare to other populations. However, the number of suicide attempts is historically high for the military and concerns us a great deal. And this number represents only those attempts we know about. To help put this in perspective, the rate of suicide attempts recorded in this population is in the same ballpark as that recorded for the highest other medical population we know about, persons with chronic renal failure who are on dialysis. This is an important areas requiring further research.

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HEARING DATE 23 Mar 89	TRANSCRIPT PAGE NO.	LINE NO.	INSERT NO. 89-09		

Mr. Wyden: In your experience with HIV-infected individuals, can you envision that a telephone-based counseling effort would be effective in addressing the mental health problems you describe?

Maj. Randell: The answer to Question 3, also applies directly to the issue raised in this question. We devote a large amount of time in the military attending to the large and growing mental health needs of the active-duty and medically retired HIV-seropositive population. It is difficult to envision accomplishing the necessary interventions by telephone. When Air Force personnel are psychiatrically examined at their annual medical evaluation and need follow-up at their home base, we are able to set up that appointment over the phone. However, before making the necessary call we have completed a face-to-face examination of the individual, know he is not an imminent risk to himself or others, are very familiar with the military mental health referral resources, and don't do counseling over the phone. I am not aware of medical precedent for this type of activity. Suicide hotlines may come the closest, but they are resources of last resort, not first resort.

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